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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Stanley E. James	Charm Bowden	Boston, MA 02110 North Scituate, RI 02857

Additional inventors are being named on the 1 *separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

METHOD AND DEVICE FOR HEATING BIOLOGICAL FLUIDS

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ENCLOSED APPLICATION PARTS ***(check all that apply)***

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Respectfully submitted,

SIGNATURE Leslie Meyer-Leon

TYPED or PRINTED NAME Leslie Meyer-Leon, Esq.

TELEPHONE 508-790-9299/Fax 508-790-1955

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PROVISIONAL APPLICATION COVER SHEET
Additional Page

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Docket Number 0656-027US1

INVENTOR(S)/APPLICANT(S)

Given Name (first and middle [if any])	Family or Surname	Residence (City and either State or Foreign Country)
James	Farago	Salisbury, NH 01952
Richard	Skiffington	North Reading, MA 01864
Kevin	Macmillan	Groton, MA 01450

[Page 2 of 2]

Number 2 of 2

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PROVISIONAL PATENT
0656-027US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Stanley E. Charm et al.

Docket No.: 0656-027US1

Title : **METHOD AND DEVICE FOR HEATING BIOLOGICAL FLUIDS**

Commissioner for Patents
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Method and Device for Heating Biological Fluids

Background of the Invention

It is desirable to sterilize, pasteurize or otherwise heat treat heat-sensitive material such as biological fluids and/or protein preparations, for example blood plasma, serum, immunoglobulins, tissue culture, or tissue-type or other material, by heating such heat-sensitive material to high temperatures for very short time periods without diminishing desirable properties of the material. U.S. Pat. No. 4,839,142, issued Jun. 13, 1989, and U.S. Pat. No. 4,975,246, issued Dec. 4, 1990, describe high temperature, short time heating of biological materials to destroy any undesirable microorganisms, pathogens, and/or viruses in the sample without substantially degrading the material itself. The heat-sensitive material is heated rapidly by microwave energy to a selected temperature, held for a very short holding time, and then rapidly cooled and recovered. Typically, the material is heated to a pre-selected temperature at which the rate of reduction or destruction of undesirable micro-organisms is greater than the rate of destruction of the heat-sensitive material itself, using microwave energy to accomplish the rapid heating. After inactivation, the material is cooled rapidly so as to stabilize the material.

One area in which the use of continuous, high-temperature, short-time heat treatment of biological materials has been important is in the development of methods for producing biological products such as biologics-based pharmaceuticals, vaccines, and the like. Existing systems have been used during the development stage of such product development, where sample sizes are relatively small compared to the batch sizes expected in production-scale processing. One existing system, the UltraTherm® system of Charm Bioengineering, Inc., is equipped with a 5 kW power supply and 2450 megahertz ("MHz") microwave generator ("magnetron"). The UltraTherm® is capable of processing only about 60 liters per hour, because the flow rate is limited by the available power. It is conventional to process complete batches within a single work-day (typically 5-8 hours), so the flow rate of existing systems limits the usual batch size to

about 300 liters per day, far below the batch sizes desired for production-scale manufacturing. (See also U.S. Pat. No. 5,389,335, issued Feb. 14, 1995, hereby incorporated by reference.)

It is therefore desirable to provide a system for the continuous, high-temperature, short-time heat treatment of biological materials that is suitable for large scale production at rapid flow rates. It is further desirable to provide a system for continuous, high-temperature, short-time heat treatment of biological materials that has design features optimized for modern production facilities.

Summary of the Invention

Disclosed is a system for thermal processing of a heat-sensitive fluid material utilizing a source of microwave energy having a frequency of greater than about 850 MHz, preferably greater than 1000 MHz, most preferably 2450 +/- 50 MHz, and a power supply of greater than 10 kW, in the range of 10-100 kW, preferably 20 kW, 30 kW, or 40 kW. The system includes a means for providing a flow stream of a heat-sensitive fluid material, the flow stream having a flow rate of greater than 80 L/hr and a waveguide in microwave communication with the source of microwave energy, the waveguide is adapted to receive a flow path for said flow stream within the waveguide. The system further includes means for monitoring and controlling the processing by the system. The means for monitoring and controlling can include a user interface located remotely. In an embodiment the system includes the power supply contained within a power supply module and also includes means for moving the power supply module to a location remote from the said wave guide and means for electronically communicating with the means for monitoring and controlling system processing. The system can also include means for pre-heating the heat-sensitive fluid material in the flow stream and means for cooling heated material. A utility module can also be included to provide a source of heat for pre-heating and a source of coolant for the coolant means. The utility module can include means for electronically communicating with the means for monitoring and controlling said processing by said system and can be remote from the microwave

waveguide. The system also can include means for cooling said heat-sensitive fluid material in said flow stream. The system can include means for measuring directly the temperature of said fluid stream.

The system can include means for monitoring and controlling leakage of microwave energy from the waveguide including multiple clamps attached to a single bar characterized in that clamping and unclamping of said multiple clamps is leveraged using said single bar. The means for monitoring and controlling leakage can include an air impermeable pressure window at the top section of a waveguide below the cover to the waveguide which cover sits on top of an applicator (microwave cover). Within the applicator can be included a conductive gasket and a quarter wave choke.

The system can be designed to accommodate a flow stream with a flow rate of at least about 300 liters/hour. The flow stream flows through the waveguide within tubing secured to a removable plate.

Also disclosed is a method of thermally reducing a micro-organism or pathogenic agent in a fluid sample of a heat-sensitive material, the method including the steps of: providing a heat-sensitive fluid in a fluid flow stream having a flow rate of greater than 80 liters per hour; b) exposing the fluid flow stream to microwave energy of greater then 1000 MHz for a pre-selected time, for example less than 0.5 seconds, sufficient to raise the temperature of the fluid in the flow stream to a pre-selected temperature so as to reduce or inactivate the micro-organism or pathogenic agent without substantial alteration of desirable properties of the material in said fluid; and c) rapidly cooling the fluid flow stream. In an embodiment, the method includes utilizing a frequency of microwave energy within the S band spectrum, for example about 2450 +/- 50 MHz.

An embodiment of the invention is a 30 kW, or more than 30 kW, microwave system for high volume processing at temperatures and times that inactivate viruses, or in some cases bacteria, but retain the favorable biological properties, such as protein activity, of the material being processed. Such a system can also be operated at times and

temperatures sufficient to sterilize biological fluids. The acceptable maximum time temperature profile depends on the stability of the biological product being processed, the buffers used and the amount of heat required.

The invention also relates to a method of achieving multilog reduction of pathogens such as viruses in a manufacturing environment requiring large volume processing, and, therefore, large flow rates of biological fluids.

The invention also relates to providing a 30 kW microwave system at flow rates of about 300 to about 450 liters per hour. Such a 30 kW system provides ultra rapid heating and cooling to maintain the biological properties of proteins while destroying viruses.

It is another object of this invention to provide a cost efficient method for removing and replacing the portion of the flow path exposed to microwave heating. If the microwave section of the flow path clogs or is contaminated it needs to be replaced. Costly flow paths, or flow paths that cannot be easily removed, are undesirable. One aspect of this invention is an inexpensive and easily removable flow path cartridge. The cartridge can be constructed of for example 316 stainless steel. Attached to and extending downward from the stainless steel plate is tubing, for example Teflon tubing, wound through microwave transparent plastic.

The rates of destruction of viruses compared to proteins favors heating biological fluid to maximum temperature for the shortest period of time possible. A system taking advantage of this phenomenon is described in U.S. patents 4,839,142, 4,975,246, 5,389,335, and 5,539,673, each of which is hereby incorporated by this reference in its entirety. See, also, Charm et al. High-Temperature Short-Time Heat Inactivation of HIV and Other Viruses in Human Blood Plasma, Vox Sang 1992; 62:12-20.

Another aspect of the invention is a system for processing biological products at high flow rates, of about 300 liters an hour to about 450 liter per hour, through a 30 kW/2450 MHz magnetron. To heat fluid evenly throughout the system, it is preferable to maintain

turbulent flow. To maintain turbulent flow, the internal diameter (ID) of the various portions of the flow path exposed to heating and cooling conditions must be minimized. Thus, it is an object of the invention to provide a system capable of uniformly heating biological fluids to high temperatures for ultra short times. To maintain turbulent flow, and maximize temperature heat exchange, the ID of the various flow paths is minimized at critical points. At high pressures, depending on specifications of the various portions of the flow path, there is a risk of fluid pathway rupture. As a result, while minimizing the ID of the various flow paths sections, system pressure changes must be minimized.

It is another object of this invention to provide a heating system in which system pressure is optimized by directing increased flow rates and, therefore, pressure changes to the portions of the flow path in which the heat sensitive material being processed is most vulnerable to denaturation. For example, utilizing tubing within system cooling sections generally with a smaller ID than in heating sections.

Another aspect of the invention is the modular design of the system. In the modular system various components of the complete system are maintained remotely. Several different modules of the system can be maintained remotely. For example, the fluid processing unit, the utility unit, the power supply unit, the central processing unit, and the supervisory controls unit can all be maintained separately and in a remote location, for example a separate room. Alternatively, all such units can be maintained together. Use of modular components confers significant advantages when using the system in a production suite having limited floor space. It such cases, certain modules, such as one or both of the power supply module and the utility module, can be moved to remote locations while remaining functional and/or electrically integrated portions of the system.

Another aspect of the invention is a 30 kW driven microwave system that can approximate the heating and cooling conditions of a smaller system such as a 5 kW driven microwave system. Such a system will allow easy scale-up of successful research and development, utilizing the smaller for example 5 kW system, to high flow rate processing.

Another aspect of the invention is a microwave heating system that includes ultra-sensitive pressure sensors within a waveguide that emit signals in the case of potential leaks. Such a pressure sensing system can include an air or inert gas inlet. Small leaks will cause pressure loss and system shut down.

Another aspect of the invention is a multi-clamp system. In an embodiment, the multi-clamp system is used for tightly sealing a cover plate over a waveguide. Such a multi-clamp system can be used in conjunction with a highly sensitive pressure change sensor and proper system sealing and grounding to prevent microwave leakage from the waveguide or applicator. The multi-clamp system can be used to help control microwave leakage. The clamps are attached to a single bar and the bar is used as a lever for clamping and unclamping of multiple clamps at one time.

Definitions

By fluid processing unit we mean the portion of the system in which heating and cooling of product occurs.

Funnel plug means a reducing fitting or adapter designed to be positioned between tubing of varying diameter and to provide a smooth transition to minimize system pressure changes.

By power supply unit we mean the power supply providing energy to the magnetron.

By parameter check section we mean the portion of the fluid processing unit between the inlet valve and the preheat heat exchange containing various sensors which record and check fluid and fluid flow after fluid enters the fluid processing unit, checks for air bubbles, and checks for fluid pressure prior to fluid entering the preheating section of the fluid processing unit.

By supervisory control unit we mean the hardware and software containing the operator interface.

Autotuner means the mechanism attached to a waveguide and projecting within a waveguide that automatically adjusts the microwave field to cause energy reflected from the microwave cover at the end of a waveguide to be re-reflected back to the load.

Dummy load means the section of a waveguide that receives and absorbs energy not absorbed by the load and which is reflected back toward the magnetron and diverted by an isolator to the dummy load.

Waveguide means a microwave chamber through which microwave energy is propogated from a magnetron to the tubing extending downwardly from the applicator.

Applicator means the top of a waveguide that sits above the top flange of the waveguide and on top of which the microwave cover is clamped. The tubing exposed to the microwave extends downwardly through the applicator into the waveguide.

Magnetron means microwave generator.

By cartridge we mean an MW cover including tubing, for example Teflon or PEEK tubing, designed to extend into the waveguide and in which process fluid flows for exposure to microwave energy.

Detailed Description of the Invention

In an embodiment, the system is an entirely self-contained, GMP compliant, continuous flow, high temperature short time microwave heating system with complete computer controls and safety interlocks. Pumps, heat exchangers, valves, tubing and instrumentation can be built on mobile stainless steel frames with wheels. Stainless steel and disposable components ease maintenance. The system can be PLC controlled and operated by the user through an advanced touch screen display featuring hierarchical

organized screens which provide all primary control parameters. System software protects against improper operation. The process screen gives a flow chart view of the system with most major parameters displayed in real-time.

The microwave energy is produced by a magnetron tube and fed through a waveguide to a microwave applicator. A specially configured coil, for example of Teflon or PEEK, is positioned inside the high intensity microwave field to achieve maximum energy transfer to the fluid and uniform heating and thus the highest temperature in the shortest time. Hold times at the peak temperature may be varied by flow rate. The final fluid temperature is monitored by either or both a non-intrusive infrared temperature sensor and RTD and is controlled by adjusting the output power of the magnetron.

In an embodiment, product is drawn through an autoclavable pump stage into a first heat exchanger where it is preheated. Subsequently it passes through the microwave field where the temperature is rapidly raised, destroying viruses. Then the product flows into one or more cooling heat exchangers where it is rapidly cooled, halting product destruction.

Precisely controlled valves allow switching between the product and a flushing solution to accurately control the recovery of the virus-inactivated product.

The system is designed to meet the throughput requirements of today's high volume production facilities in a throughput capacity of, e.g., 360 liters per hour. The system is highly automated and user friendly. The system is modularized to maintain a small footprint in the expensive production suite. System components including the microwave power supply and utilities modules and control module can be remotely located. Remote modules are networked and computer controlled. The stainless steel microwave module, with hinged doors all around for accessibility, is easy to maintain and clean. The waveguide section is interlocked with redundant safeties. Features of the system include about 300 to about 450 L/H continuous throughput; ultra short time heating; 6 log viral reduction capabilities; minimal product loss; accurate and repeatable temperature control;

2450MHz microwave technology; industrial grade components throughout; no chemicals to remove; no clogged filters to replace; small footprint in the manufacturing suite; and three piece modular movable system.

One embodiment of the invention is a modular system for heat treatment of biological fluids at increased flow rates. In an embodiment of the invention a modular design allows the fluid processing unit to be separated from other portions of the system. By such a separation, the fluid processing unit can be isolated, for example in a temperature, humidity or other controlled environment room. The fluid processing unit contains all product contact points. As a result, the strict sanitation requirements relative to components that contact pharmaceuticals products and raw materials, need not be applied to such remote units, thereby saving time and expense.

The modular design also allows for sharing of costly components. For example, in embodiments utilizing a microwave heating system, one power supply unit can be alternated between two or more fluid processing units. Doing so also decreases down time during switch over from one product to another or during cleaning. In addition, sharing of fluid processing units allows for a more cost effective approach to avoiding cross-contamination between products. For example, one fluid processing unit can be assigned to one particular product while a utility unit or power supply unit can be shared.

The modular design of the system is even more critical when large magnetrons are used. For example, 895 or 915 MHz frequency magnetrons may require more physical space than a 2450 kW frequency magnetron. For example, 895 or 915 MHz magnetrons can utilize somewhat larger power supplies, for example up to 100 kW whereas 2450 kW frequency magnetrons can currently utilize power supplies in the range of 1 kW to 30 kW.
Physical space requirements may necessitate moving modules into separate rooms.

In an embodiment the modular system includes three modules: the power supply unit, the fluid processing unit and the utility unit.

Power Supply Unit

In one embodiment, the power supply unit can include four identical 12 kW inverter modules, creating a 48 kW power supply unit. As such, the power supply is itself modular; each 12 kW inverter module can operate independently. One inverter unit at a time can be replaced. In this particular embodiment, the power supply includes four identical but separate switching power supplies with parallel outputs. Each module converts 480 volts alternating current (480 vac) into 16.7 kV direct current (16.7 dc) at 2.45 amp. It will be appreciated that although a 48 kW power supply is used with a 30 kW magnetron, a smaller power supply is sufficient for a lower kW magnetron. For example, three or even two 12 kW inverter modules could be used to operate a 20 kW magnetron. Similarly, a larger power supply would be required for a larger magnetron. In particular, magnetrons operating at 915 MHz tend to be larger than those operating at 2450 MHz. Alternatively the power supply unit can include a single inverter module as the full power source.

Whether the power supply includes a single inverter module or several linked together, it can be provided in a housing separate from the fluid processing unit. The power supply can be provided on a skid with wheels for easy movement. In an embodiment, a single power supply or sub-modules of a single power supply can be used to operate multiple fluid processing units. In that way, the cost of purchasing several systems can be reduced, the flexibility in the size of the space allocated to the fluid processing unit is increased and the cleaning requirements for the power supply will not be as stringent as that for the fluid processing unit.

In one modular embodiment, the power supply receives instructions from the supervisory control unit over a network, e.g., a Profibus network, through a high voltage cable and supplies power to the magnetron over a filament and magnet control cable.

Utility Unit

Adding to the modularity of the system, the utility unit, including both coolant fluid sources and optional heating fluid sources, can be provided separately from the other system modules. For example, the utility unit can be remote from the fluid processing unit, such as in a separate room or the same room apart from the fluid processing unit. In addition, as with the power supply unit, one utility unit can be used to operate separate fluid processing unit.

In a modular embodiment, the utility unit receives instructions from the supervisory control unit over the Profibus network through a cable.

In an embodiment the utility unit is on wheels as a unitary, movable unit. In this embodiment, the utility unit includes two parallel sides: the heating side and the cooling side. Each side can be a self-contained closed loop system with coolant to the system supplied by an independent cooling source, for example cold water/glycol or coolant water, through heat exchangers. In an embodiment, multiple closed loop coolant or heating systems can be included. In a particular embodiment described herein, there are two coolant loops and one heating loop.

Cooling Loops

The cooling portion of the utility unit can include one or multiple coolant supply reservoirs. In a particular embodiment, two coolant reservoirs are provided: one to supply the heat exchangers that cool the fluid leaving the microwave (primary coolant loop) and one to supply cooling fluid to other components of the system requiring cooling (secondary coolant loop).

In an embodiment, the primary coolant loop includes a coolant mixture known to those skilled in the art, e.g., a coolant liquid that is a mixture of 90% deionized water to 10% glycol. Various combinations can be used including 100% deionized water. The primary coolant loop is a closed loop system including a coolant liquid reservoir. In an

embodiment for processing large volumes, for example in a 30 kW system, the reservoir capacity is approximately 400 cubic inches. Reservoir size can easily be adapted to changes in system requirements. Liquid flows from the reservoir to the suction side of a pump, for example a magnet pump. From the pump, fluid flows through a heat exchanger, to cool the fluid exiting the reservoir, containing coolant such as chilled water from an external source. The fluid then flows from the utility unit to the fluid processing unit. In an embodiment, the fluid processing unit utilizes the primary coolant loop fluid only to cool heated material leaving the applicator/waveguide of the fluid processing unit. The cooling of the heated material is accomplished using heat exchangers such as plate heat exchanger or other heat exchanger adapted to the particular requirements of the system. In another embodiment, the primary coolant loop also provides coolant to an optional micro-cooling heat exchanger positioned between the outlet of the applicator/waveguide and the inlet to the cooling plate heat exchanger.

After flowing through the cooling plate heat exchangers of the fluid processing unit the primary coolant loop fluid returns to the utility unit. Upon return from the fluid processing unit the fluid can flow through a flow meter, to verify proper pump functioning prior to flowing back to the reservoir. Within the reservoir two level switches can be provided to monitor both maximum and minimum desired fluid levels.

In an embodiment, a secondary coolant loop includes, e.g., a mixture of 90% deionized water to 10% glycol. Such a secondary coolant loop can be used to provide coolant to either multiple parallel cooling circuits or, alternatively, a continuous flow series loop. The advantage of parallel cooling circuits is that fluid temperature to each parallel circuit is similar as compared to circuits in series in which fluid first flows from one cooling circuit to the next, absorbing heat but not substantially dissipating heat. In both the parallel and series cooling circuit design, coolant flows to each cooling circuit separately and then is recirculated back to the reservoir.

The secondary cooling loop can begin from a reservoir to the suction side of a secondary coolant loop pump, such as a pump identical to that used for the primary cooling loop, and then leaves the utility unit and enters the fluid processing unit.

Within the fluid processing unit in a multiple parallel cooling circuit embodiment, the secondary coolant loop includes: 1) magnetron tube cooling circuit; 2) applicator cooling circuit; 3) auto-tuner cooling circuit; 4) cabinet air cooling circuit; 5) dumby load cooling circuit. It is possible also to include a circuit to the optional micro-cooling heat exchanger positioned between the outlet of the applicator and the inlet to the cooling plate heat exchanger. Within each cooling circuit can be multiple branch cooling circuits. In an example of a microwave system including an auto-tuner, the auto-tuner cooling circuit itself includes multiple branch cooling circuits, for example, above and below the auto-tuner. In addition, in microwave systems an outlet for unabsorbed microwave energy (heat) can be provided, known as a dummy load. What is known in the art as a microwave isolator is used to shunt reflected power to the dummy load. The cabinet air-cooling circuit includes fans to blow cool air off the cooling circuit and into the cabinet.

All coolant loops can have temperature sensors to verify the temperature of the coolant. For example, a resistance temperature device (RTD) can be used to measure temperature of the coolant fluid. In one embodiment, an RTD is situated prior to the entry of the secondary coolant loop fluid to the magnetron tube cooling circuit. Efficient placement of RTD's in general can be directed to the most vulnerable locations requiring coolant, for example the locations generating the most heat such as the magnetron tube. RTD's can also be located in what are known in the art as thermowells. Placement within thermowells allows movement of RTD's from one location to the next without disrupting coolant flow. Fittings, such as Swagelock fittings, can be used to secure RTD's into the various thermowells.

Various flow switches can be included through the cooling and heating flow to verify proper system performance. For example, flow switches can be included around the magnetron tube cooling circuit, the auto-tuner cooling circuit and the dumby load cooling

circuit. To avoid damage to the equipment and/or injury to personnel, lack of adequate fluid flow through a cooling circuit automatically shuts the system down.

A third or more cooling loops can be provided if necessary, particularly if one or more areas require fluid at different temperatures than other areas. In an embodiment a third cooling loop provides coolant to an air conditioning unit within the microwave control and power supply.

Pre-Heating Loop

In an embodiment a pre-heating loop is provided. The pre-heating loop provides hot water to the preheat plate exchangers of the fluid processing unit. In an embodiment, the pre-heating fluid is stored in a reservoir with capacity of approximately 400 cubic inches. Fluid leaves the reservoir and enters the suction side of a pump where it is pumped to a heater such as an electric resistance heater or gas heater. Heated fluid flows from the heater by an RTD that checks the temperature of the heated fluid. Heated fluid flows off the utility unit and into the preheat plate exchangers of the fluid processing unit. After utilization in the plate heat exchangers fluid flows through a flow meter and back to the reservoir.

The pre-heating loop provides the initial heating, within the fluid processing unit, prior to microwave heating. Such a pre-heating loop is optional; all heating can occur within the microwave portion of the system. Providing a heat exchange pre-heating loop increases the efficiency of the system and maximizes the peak temperature achievable at a given flow rate with a given power supply.

The critical portion of the heating within the fluid processing unit begins at the temperature above which protein denaturation, of the particular protein being processed, occurs. Above the temperature at which denaturation occurs, rapid heating is critical. Below the temperature at which denaturation occurs a longer heating time is acceptable.

Thus, utilizing a plate heat exchange element, fed by a heated fluid loop, allows more microwave power to be used for maximum rapid heating above the critical temperature. For example, it may be most efficient to utilize the pre-heat heat exchanger to bring the fluid temperature to just below the temperature of significant protein denaturation. After reaching that temperature, rapid heating in the microwave can be used to avoid denaturation, partially or wholly. Parameters chosen will depend on the particular protein solutions, stabilization buffers used and target virus or bacteria.

Fluid Processing Unit

In an embodiment, the fluid processing unit generally includes stainless steel 316 tubing through which product flows. Various size triclamp fittings, sanitary valves and sanitary adapters provide connections within the generally stainless steel flow path. Alternatively the flow path could include Teflon or other flexible material such as silicon or latex. The choice of material will partially depend on requirements such as necessity that the flow path be autoclavable and the maximium pressure requirements of the system and maximum pressure specifications of the various materials.

The fluid processing unit can have multiple processing inlets valves, for example solenoid inlet valves. In an embodiment including three inlets, at least one inlet is for product and at least one inlet is for saline. Both inlet sources can be maintained remote from the fluid processing unit or adjacent to the fluid processing unit. Solenoid valves can be used to control the source of fluid whether from the product inlet or saline inlet. Fluid flow for processing is from one or the other inlet through the solenoid or other shut off valves into the suction side of a pump controlled by a variable speed drive.

In an embodiment, fluid flows out from a pump into a parameter check section including, for example: a bubble sensor using ultra sound to determine changes in fluid; a magnetic flow meter, such as a 3/8 inch ID magnetic flow meter connected to a signal converter; a pulsation dampener; a pressure sensor, a triclamp flange connections. The pressure sensor measures the pressure in the flow path of the system immediately prior to fluid

entering the pre-heat loop. Undesirable pressure measurements at this point in the system can trigger the system to shut down. Fluid can next pass an RTD to measure the temperature of the fluid prior to fluid entering the processing section. Various of the system can be automatically or manually adjusted to accommodate varying temperatures of fluid entering the system.

In an embodiment, the processing section of the fluid processing unit includes: an optional preheat unit; microwave applicator unit; an optional pre-coolant unit; coolant unit. Although the preheat unit is optional, it is highly desirable to maximize heating efficiency of the magnetron.

In an embodiment, the preheat section includes a flat-plate heat exchanger. In another embodiment, the preheat section includes a tube in shell heat exchanger or other heat exchangers known in the art. In either embodiment, heating fluid is provided from the pre-heating loop of the utilities unit.

In an alternative embodiment, no pre-heat section, and therefore, no utility unit pre-heat loop is required. In such an embodiment, all heating is accomplished by a microwave source. Depending on the peak temperature and speed to peak temperature requirements, such a non-preheat system may or may not be practical.

After exiting the pre-heat unit, fluid temperature can be measured by an RTD that measures the temperature of the fluid after heating in the pre-heat unit. An RTD provides a signal, through a programmable logic controller, that controls the speed of the hot water pump. If the pre-heat is not providing sufficient heating of the fluid, the pump speed of the utility unit pump can be increased and if the pre-heat is overheating the fluid, the pump speed can be decreased. Alternatively, but generally less desirable, flow rates through the pre-heat section can be adjusted to provide adequate pre-heating.

After preheat, fluid flows to the waveguide beneath the applicator. After heating in the microwave applicator unit, fluid passes an infrared temperature sensor prior to entering

the coolant unit. Alternatively, fluid passes an RTD prior to entering the coolant unit. An RTD can be used in conjunction with an IR sensor or alone.

In an embodiment, the coolant unit includes a flat-plate heat exchanger. In another embodiment, the coolant unit includes a tube in shell heat exchanger or other heat exchangers known in the art. In either embodiment, coolant fluid is provided from the primary coolant loop of the utilities unit.

It has been found that in ultra short time heating and cooling, the cooling step can be the most critical. The residence time in the microwave is relatively brief, for example, less than one-half second. After fluid product leaves the waveguide/applicator it is cooled. It is the amount of time a product stays above the temperature at which it is stable that determines total product destruction. Thus, after an optimum time temperature profile is determined for product and virus, it is critical to control the cooling of the product so that the optimum is reached. Plate heat exchangers are one method of rapid cooling. Tube in shell cooling is another method of rapid cooling. In both cases it is preferable to maximize the surface area of the fluid exposed to the coolant. Another possible method of rapid cooling utilizes vacuum cooling. Still another method of cooling utilizes plate heat exchangers with a low viscosity fluid. Such a low viscosity fluid can provide an increased heat transfer coefficient and, therefore, more rapid cooling.

It is optimum to begin cooling immediately after fluid exits the applicator/waveguide. In an embodiment, in which plate heat exchangers are located some inches away from the outlet from the waveguide/applicator, an additional micro-cooling heat exchanger can be provided as a pre-coolant unit. Such a pre-coolant unit can be designed to provide heat exchange cooling of fluid immediately after exit from the microwave applicator unit and prior to entering the coolant unit. The pre-coolant unit can be 316 stainless steel, designed in a cylindrical shape and include, for example, a 1/8 inch ID flow path surrounded by a chamber containing coolant. In another embodiment the pre-coolant micro-cooling heat exchange unit includes for example cryogenic oil for rapid cooling.

In another embodiment, the micro-cooling heat exchanger can be fed by a separate chiller to provide fluid at lower temperature than is provided other components of the system.

After exiting the coolant unit, an RTD can be used to provide an additional fluid temperature record. Fluid then is either sent to waste or product depending on the setting on shut-off valves leading to product and waste.

Fluid Path

Fluid flows into the fluid processing unit from either a separate remotely located inlet source module or from inlet containers adjacent to the fluid processing unit. Fluid flows in from the inlet through tubing of, for example, 1 inch ID or ½ inch ID. In an embodiment, fluid flows within the fluid processing unit through a 316 stainless steel flow path. In one embodiment, the stainless steel flow path is about 1/8 to about ½ inch internal diameter, for example 3/8 inch ID. Fluid flows in the three-eight inch ID stainless steel flow path through a pump and then through a parameter check section such as described above including a bubble sensor employed external to the flow path. In an embodiment, a portion of the stainless steel flow path is replaced with a plastic flow path section, for example of polypropylene, around which the bubble sensor is employed. In this embodiment, fluid flows by a flow meter and pressure transducer and RTD before entering a pre-heat unit. In an embodiment using pre-heat plate heat exchangers, fluid flows from a 3/8 inch ID stainless steel flow path into a cone shaped 3/8 inch ID sanitary adapter leading to the inlet of a pre-heat plate heat exchanger. The 3/8 inch ID sanitary adapter is employed to allow leak-proof transition to the relatively wide inlet of the preheat heat exchanger while avoiding excessive system pressure fluctuation.

After flowing through the plate heat exchangers fluid re-enters the system flow path. The outlet from the plate heat exchanger can be fitted with a cone-shaped funnel plug with a taper. For example, a funnel plug with a 60 degree taper to 1/8 inch ID. Alternatively, a funnel plug can taper to a wider diameter if the tubing leading to the microwave is widened. The funnel plug is adapted to minimize pressure changes within the system as

fluid flows from one diameter flow path to another. In an example in which the exit of the funnel plug is 1/8 inch ID, fluid flows from the funnel plug into a 1/8 inch ID length of tubing leading to the applicator/waveguide. The smaller ID length of tubing, for example 3/8 inch ID, prior to the larger ID tubing, for example 1/4 inch ID tubing within the microwave, is used to minimize hold time at the elevated temperature fluid reaches within the pre-heat heat exchanger. This 1/8 inch ID section may be optional depending on the sensitivity of the fluid at the temperature leaving the pre-heat. If the fluid components are stable at the temperature, fluid may flow instead directly into a tubing of internal diameter (ID) matching the ID of the tubing extending from the MW cover into the waveguide.

Fluid flows from the optional 1/8 inch ID tubing into the tubing of, for example ¼ inch ID tubing within the waveguide. Fluid leaving the waveguide passes into T-fitting with a 1/8 inch ID flow path and an RTD inlet. An RTD at the T-fititng RTD inlet can be redundant to the IR sensor and can be used for calibrating the IR temperature sensor or, in an embodiment, to replace the IR temperature sensor. The 1/8 inch ID flow path includes a micro-cooling heat exchange section to immediately begin cooling of fluid prior to entering the cooling plate heat exchangers. Said micro cooling heat exchanger can be cylindrical in shape. Connecting the micro heat exchanger to the T-fitting is a ½ inch sanitary connection secured with a triclamp. Fluid exits the micro heat exchanger through a funnel plug in reverse position from the funnel plug utilized at the exit from the preheat heat exchanger. Fluid enters the funnel plug through a , for example, 1/8 inch ID opening and exits the funnel plug through the tapered end into the inlet of the cooling plate heat exchanger. Upon leaving the plate heat exchangers, fluid (for example, 1/2 inch sanitary connection secured by triclamp into 3/8 inch ID stainless steel tubing) passes by an RTD which measures the temperature of the cooled fluid.

It will be appreciated that the flow rate in the range of about 300 to about 450 liters per hour through tubing ranging in size from 1 inch ID or ½ inch ID to 1/8 inch ID or less requires adaptation to avoid excessive pressure changes within the system. The series of sanitary fittings and adapters with tri clamps can be used to move within some range of

ID. To minimize pressure variations, however, the funnel plugs and various other adapters can be used to optimize system performance.

In general, it is optimal to minimize system pressure drops. Funnel plugs provide a mechanism to reduce system pressure drops when moving fluid from a larger ID tubing section to a lower ID tubing section. Maximum pressure within the system is limited by the specifications of various components of the flow path. If pressure drops must occur, it is generally beneficial to focus such pressure drops at portions of the system in which maximum flow rate is most critical. For example, on the one hand, protein denaturation may be limited or non-existent at system pre-heat temperatures and times. As a result, it may be optimum to minimize system pressure changes in the pre-heat section and allow longer residence times in the pre-heat section. On the other hand, to the extent protein denaturation occurs it will generally occur at a higher rate around peak temperature. To minimize denaturation, and maximize control over the time temperature profile, cooling efficiency should be optimized, for example by maximizing flow rates through the cooling sections. One method for maximizing flow rates in the cooling section is to minimize the ID of the tubing in that section. Although the result will be a system pressure drop, system pressure will have been put to maximum advantage.

Figure 1 is a detailed drawing of the micro-cooling heat exchanger 1 between the outlet 2 from the waveguide 110/applicator 70 (see fig. 11) and the inlet 3 to the cooling plate heat exchanger 4. Fluid is heated first by the pre-heat heat exchanger and then passes into the tubing extending into the waveguide from the MW cover 5. After exiting the tubing fluid is heated to peak temperature. It is desirable to begin cooling immediately upon exiting the tubing. Fluid exits the tubing through a T fitting 6 and enters the fluid pathway 7 within the micro-cooling heat exchanger 1. Fluid then enters the funnel plug 8 prior to entering the cooling plate heat exchanger 4.

Figure 2 is an iso drawing of micro-cooling heat exchanger 1 including flow path 7 surrounded by hollow space 20, 21 through which coolant fluid is pumped from either the primary or secondary coolant loops or an alternative coolant loop.

Figure 3 is an iso drawing of a funnel plug 8 with a one-eight ID enter/exit port 30. The funnel plug 8 can be constructed of 316 stainless steel. The flow path through the middle of the funnel plug 8 becomes part of the flow path of the fluid processing unit 120 (see fig. 12). The 1/8 inch ID port 30 end of the funnel plug is secured using sanitary fitting to connecting sections of the fluid path of the fluid processing unit 120. In an embodiment, the funnel plugs 8 are used to adapt to the change in ID: a) at the outlet from the pre-heat plate exchanger; and b) at the inlet to the cooling heat exchanger 4 (see figure 1). The outlet from the pre-heat plate heat exchanger is a larger ID space than the entrance to the flow section leading to the applicator/waveguide. The tapered end 31 of the funnel plug 8 guides fluid flow from the outlet of the pre-heat to the 1/8 inch ID flow path leading to the applicator 110/waveguide 70. In another embodiment, the funnel plug 8 includes a 1/4 inch ID flow path adapted to guide fluid into a one-quarter inch flow path leading to the applicator 110/waveguide 70.

Figure 4 is a drawing of the tapered end 31 of a funnel plug 8 including 60 degree taper 40 gasket 41.

Figure 5 is a detailed drawing of a funnel plug 1 showing the sixty degree funnel section 40 opposite the port 30.

Applicator/waveguide

The fluid inlet to the applicator/waveguide within the fluid processing unit can be through a tee fitting on top of which is an RTD port. The tee is secured to the applicator cover (MW cover) that is secured to the top of the applicator and both covers the waveguide and secures the tubing within the waveguide.

The MW cover is designed to both prevent microwave leakage from the applicator/waveguide and secure the tubing for product flow within the applicator/waveguide. The MW cover can be, for example, a ½ inch thick aluminum

plate. The MW cover is secured to the applicator via series of clamps. Said clamps can be either single clamps or connected in series. Connecting the clamps together allows efficient removal of the MW cover, provides a lever for undoing the clamps and provides and efficient mechanism to assure even, tight clamping. In an embodiment the clamps, for example a series of two, three or more clamps, are connected by a solid material, for example metal or hard plastic bar through which a screw is placed to fasten each individual clamp (multi-clamps). In another embodiment a second bar is secured to another location on the clamps. One bar is used to release the clamps and another bar is used to lift the clamps off the MW cover.

The MW cover is secured on top of the applicator. On the bottom side of the MW cover is the tubing that is exposed to microwave energy. In an embodiment, the tubing is about 25 inches to about 100 inches, for example 50 inches, and varying ID, for example about 1/8 inch ID to about ½ inch ID, for example ¼ inch ID. The diameter and length can be varied within a range to accommodate desired increases or decreases in exposure times within the waveguide. In an embodiment, the tubing is made of Teflon. In another embodiment the tubing is made with polyether ether ketone (PEEK).

U.S. patent 5,389,335 describes a prior art disposable cartridge including a tube in shell preheat and cooling heat exchangers (figures 2 and 3). The cartridge described in 5,389,335 had the disadvantage of having the heat exchangers attached thereto and, thereby increasing the cost of the cartridge. Multiple cartridges will be required by a user and, therefore, decreasing the cost of each cartridge is important. In an embodiment, the cartridge includes the MW cover and tubing only. Said tubing can be wound vertically as shown in figures 2 and 3 of 5,389,335, or alternatively wound generally horizontally.

Providing less functionality to the cartridge reduces the cost and, therefore, increases flexibility in disposal and replacements.

An additional mechanism to prevent leakage from the applicator/waveguide is an enlarged o-ring gasket machined into the top face of the microwave applicator. Said o-

ring gasket can be a rubber o-ring gasket. The o-ring gasket provides both a pneumatic and static shield for choking microwave energy within the waveguide. Conductive material within the o-ring provides static grounding for 2450 MHz frequency. In addition, the o-ring provides a pneumatic shield to prevent air leakage out of the waveguide.

The portion of the waveguide above a pressure window is pressurized, at low pressure, with air, or an inert gas. Pressurization can be about 8 psi (8 inches water). Air or inert gas is directed into the waveguide above the pressure window. The pressure window allows pressurization within a portion of the waveguide and prevents leakage material from falling into and contaminating the microwave field possibly causing energy arcs which could damage the magnetron. The pressure window can be, for example, a quartz pressure window or, alternatively, the pressure window can be made from Teflon. The pressure window can be secured within the waveguide within a flange connection.

Pressurization within the waveguide above the pressure window allows for highly sensitive monitoring of proper system connections. It is important, to prevent and provide immediate detection of microwave leakage, that system connections be monitored. Loss in pressure within the waveguide, for example from a loose connection or insecure fitting, above the pressure window can automatically shut the system down thereby preventing microwave leakage. To create the low pressure environment, for example one-third PSI, required for sensitive leak detection, high and low pressure regulators are required with pressure switches.

Redundancy for microwave leak detection is built into some embodiments. For example, in addition to pressurization monitoring within the waveguide can be microwave leak detectors, such as interlock monitors. Further redundancy can be provided using proximity sensors to determine that system components are in place and fastened correctly. For example, a proximity sensor positioned within the applicator and below the faceplate.

In an embodiment, the magnetron is a 30 kW 2450 MHz magnetron. A WR-430 waveguide is utilized to direct microwaves to the product. The magnetron tube/waveguide assembly can be designed to operate remote from the power supply unit. The assembly can also include a circulator to direct reflected power to a dummy load, microwave tuner, such as an auto-tuner, a pressure window and a 90 degree elbow between the magnetron head and vertical portion of the wave guide.

Figure 6 is a schematic side view of 316 stainless steel MW cover 5 with inlet 60 and tubing 61 extending downwardly from the MW cover 5, wound generally horizontally through preferably microwave transparent plastic holders 62 secured to the MW cover 5. Various tubing lengths are possible depending upon the time/temperature profile and, therefore, the time required within the waveguide. Also shown is specialized T-fitting 63 leading into the tubing 61 including three separate sealing surfaces including a nut/ferrule connection 64 on top used to secure the RTD. A sanitary fitting 65 on the side provides either fluid inlet or outlet and a combination of sanitary and flange fittings on the bottom 66 secure the T-fitting to the MW cover 5.

Figure 7 is an iso drawing of microwave applicator 70 and top flange 71 with MW cover 5 in place. Multi clamps 72 on all four sides of the applicator are in the non-enaged position. Infrared sensor secured in block 73 provides temperature measurements for fluid after heating in the microwave. When secured to the waveguide, the top flange 71 is within the cabinet. Two specialized T-fitting 6/74, one inlet 74 and one outlet 6 including in each three separate sealing surfaces including a nut/ferrule connection 64 on top used to secure the RTD. A sanitary fitting 65 on the side provides either fluid inlet or outlet and a combination of sanitary and flange fittings 66 on the bottom secure the T-fitting to the MW Cover 5. Fluid enter the applicator 70/waveguide from the pre-heat heat exchanger through the inlet T-fitting 74 and exits the applicator 70/waveguide 110 through the outlet T-fitting 6 into the micro-cooling heat exchanger 1 (see figure 2).

Figure 8 is an iso drawing of microwave applicator 70 without MW cover 5 and with top flange 71 for connecting the applicator 70 to the waveguide. Multi clamps 72 on all four

sides of the applicator are in the non-enaged position. Infrared sensor inlet block 73. Proximity sensor 80 provides redundant protection against an inadequately secured MW cover 5. O-ring gasket 81 holds air pressure in for presence sensing air pressure switch and provides a conductive electrical contact for grounding and microwave choke. When secured to the waveguide, the top flange section 71 sits within the cabinet and out of view. Opening 82 is at the top of the WR-430 waveguide and is the space in which the tubing 61 (see figure 6) is placed for exposure to microwave energy.

Figure 9 is an iso drawing of MW cover 5 with microwave transparent plastic tubing holders 90. Micro-cooling heat exchanger 1 leads to the entry to the cooling plate heat exchanger 4 through a reverse position funnel plug 8. Special T fittings 6/63 provide connections from the applicator 70 (see figure 8) to the micro-cooling heat exchanger 1. Downwardly extending microwave transparent plastic holders 90 are shown without tubing 61 (see figure 6).

Figure 10 are iso drawings of multi-clamp 72 utilizing a bar 100 secured to a clamp 101 for ease of use and tight connections.

Figure 11 is a schematic of waveguide 110 starting at the magnetron box 111. Microwaves are generated by a magnetron within the magnetron box 111 and are propagated to the a ninety degree angle and up toward the applicator 70. The waveguide 110 includes several flange connections including the top flange between which is the pressure window. Microwave autotuner box 115 is attached to the waveguide 110 and includes projections into the waveguide 110 that automatically adjust the microwave field to cause energy reflected from the MW cover 5 (see figure 6) at the end of the waveguide 110 to be rereflected back to the load.

Supervisory Control Unit

The supervisory control unit can be physically attached to the fluid processing unit so that the operator stands adjacent to the unit during operation. The supervisory control unit can also be a separate module operated remotely from the fluid processing unit.

The supervisory control unit user interface can be programmed using WonderWare software. The WonderWare software communicates with the programmable logic controller (PLC) through a serial bus. WonderWare provides instructions to the PLC, for example, a Siemens 505 Series. Multiple input/output racks are controlled by the PLC. In a particular example of three input/output racks one controls the fluid processing unit, one controls the utility unit and one controls the power supply unit. All communications to the PLC can be through a Profibus network and over a network cable thus allowing multiple modules, in remote locations, to be operated by the supervisory control unit (which may be remote or physically attached to the fluid processing unit.

It will be appreciated to those skilled in the art that although a microwave system may provide the most efficient rapid heating, many aspects of this invention are applicable to other heating systems. Such an alternative heating system may utilize plate exchangers for all heating requirements. Many aspects of this invention will be applicable to such a heater including the modularity of the system and features relative to reducing pressure changes within the system.

Figure 12 is an iso view of the front of fluid processing unit 120. Fluid passes through inlet valve 121 and into motor/pump 122 via 316 stainless steel flow path 123 with sanitary fittings 124. Fluid exits a pump 122 and passes through the 316 stainless steel flow path between the pump and the pre-heat plate heat exchanger. Fluid exits the pre-heat plate heat exchanger through a funnel plug 8 and a 316 stainless steel elbow into the T-fitting 63 entry into the applicator 70/waveguide 110. Fluid exits the applicator/waveguide through a T-fitting 6 through a micro-cooling heat exchanger 1 (see for example figure 9) and into the cooling plate heat exchanger 4 (see for example figure 9). The waveguide 110 begins at the magnetron box 111 and makes a 90 degree

connection to the vertical portion. A series of flanges 125,126,127,128,113 provide inlets for coolant. An autotuner is attached to the waveguide (in box 115) with components extending into the waveguide. Waveguide ends at the top of the applicator 70 upon which is the MW cover 5 with multi-clamps 72 and downwardly extending tubing (not shown) above the top flange 71. The pressure window flange 113 holds the pressure window in place. Above the pressure window flange 113 is an air inlet for pressurizaton above the pressure window. Also shown is screen 128 for supervisory control unit, in this embodiment physically attached to the fluid processing unit.

Figure 13 is an iso side view of fluid processing unit 120. Fluid passes through one of inlet valves 121, 130, 131 and into motor/pump (not shown)via 316 stainless steel flow path (not shown). Please heat exchanger are within cover 132. Fluid exits the pre-heat plate heat exchanger through a funnel plug 8 into the T-fitting 63 entry into the applicator 70/waveguide 110. Fluid exits the applicator/waveguide through a T-fitting 6 through a micro-cooling heat exchanger 1 and into the cooling plate heat exchanger (under cover 132). The waveguide 110 begins at the magnetron box 111 and makes a 90 degree connection to the vertical portion. A series of flanges 125,126,127,128,113 provide inlets for coolant. An autotuner is attached to the waveguide (in box 115) with components extending into the waveguide. Waveguide ends at the top of the applicator 70 upon which is the MW cover 5 with multi-clamps 72 and downwardly extending tubing (not shown) above the top flange (not shown). The pressure window flange (not shown) holds the pressure window in place. Above the pressure window flange is an air inlet for pressurizaton above the pressure window. Also shown is screen 128 for supervisory control unit, in this embodiment physically attached to the fluid processing unit.

Figure 14 is a fluid flow diagram for a 30 kW system. The microwave module includes three inlets: saline, CIP and product. Fluid flows into the fluid processing unit from the inlets through a valve such as a solenoid and into the flow path of the fluid processing module. Bubble sensor checks for bubbles in the fluid and the pump drives the fluid flow through a flow meter and pressure sensor and RTD. Fluid flows into the pre-heat, heat exchanger and then past an RTD and into the waveguide where it is exposed to

microwave heating. Upon exiting the waveguide fluid passes an RTD or IR temperature sensor prior to entering a first micro-cooling heat exchanger and a secondary coolant block plate heat exchanger. Fluid exits the cooling heat exchange section, passes an RTD and a back pressure valve used to avoid fluid boiling before exiting the system through outlet valves to either product or waste containers.

Instrument air supply provides air through two pressure reducing valves and a solenoid valve into the portion of the wave guide above the quartz pressure window thereby providing low PSI pressurization used as a sensor to avoid microwave leakage. Air pressure is also supplied by the instrument air supply to the back pressure valve.

The hot water section of the utility module provides hot water, from a reservoir with high and low level switches through a pump and pressure gage and into a heater. After exiting the heater hot water flows by a first RTD and a second RTD into the preheat heat exchange block. After flow through the heat exchange block hot water circulates back to the utility module through a flow meter and into the reservoir.

Two cold water loops are diagrammed. The primary loop is diagramed as a serial flow cold water loop. The primary cold water loop can also be, and preferably is, a parallel flow loop. The cold water loop provides cold water or other cold liquid from a reservoir through a pump pressure sensor and heat exchanger where the liquid is cooled by an external cold liquid source. Fluid flows into the fluid processing unit by an RTD and into the cooling loop chambers surrounding the applicator, tuner, magnetron head, microwave control and power supply and dummy load before circulating through a pressure sensor and back into the reservoir. The secondary control loop provides cold liquid from a reservoir through a pump and pressure sensor into a heat exchanger for cooling by cold liquid from an external source. Cooled liquid then flows by an RTD and into the primary and secondary coolant heat exchangers before circulating back to the reservoir after passing a flow meter.

Throughout the system flow path are temperature test wells and pressure test connections to monitor system parameters and diagnose system problems.

Figure 15 is an iso drawing of a fluid flow path leading from the inlet valves 121, 155, 156 through 316 stainless steel flow path including sanitary fittings and elbows to pump 122 and again to 316 stainless steel flow path 123 with sanitary fittings 124 with elbows 150 to pressure sensor 153 and flow meter 154 and to sanitary adapter 151/funnel plug (not shown) inlet of pre-heat heat exchanger. It is possible to replace stainless steel in areas of the flow path with other material such as Teflon tubing.

Example 1

In a particular example utilizing a one-quarter inch internal diameter (ID) 50 inch cartridge (the portion of the fluid processing unit in which microwave exposure occurs) and a flow rate of 425 liters per hour, and 28 kW of power, thermal destruction of SV 40 virus was calculated, using MathCad, for various phases of heating and cooling.

Time in the preheat section of the fluid processing unit was 3.956 seconds. After exiting the preheat section, product flows through a preheat hold tube, of one-quarter inch ID and length of 10 inches, prior to entering the applicator/waveguide. Time in the prehat hold tube was 0.136 seconds. The total preheat time was, therefore, 4.092 seconds. Total time of microwave exposure was 0.341 seconds. From the applicator/waveguide fluid enters a 10 inch long micro-cooling heat exchanger with ID 1/8 of an inch. Fluid is within the micro-cooling heat exchanger for approximately 0.017 seconds. After leaving the min-cooling heat exchanger fluid enters the cooling plate heat exchanger. Fluid exits the cooling plate heat exchanger after approximately 5.56 seconds.

Log base 10 reduction (log reduction) of SV 40 within the system was calculated from known Arrhenius values of SV 40. Log reduction in various portions was as follows: preheat section 1.445 x 10^{-3}; applicator/waveguide 1.825; micro-cooling heat exchanger 0.659; cooling heat exchanger 6.74.

Example 2

Comparison was made between inactivation of glucose oxidase and beta-galactosidase within a 5 kW and 30 kW microwave system. Results show similar destruction profiles.

Beta-Galactosidase Assay

Materials: 1) 100 mM Na Acetate pH 5.0 (Glacial Acetic Acid and NaOH) (100 ml); 2) 20 mM ONPG solution (Sigma N1127)(50 ml); 3)0.2 M Na Carbonate (Mallinckrodt 7527) (200 ml); and 4) Cuvettes, glass tubes with stoppers, etc.

Equipment: 1) Inctronic II incubator at 37C (both sides); 2) Spectrophotometer set at 420nm and zeroed with water; and 3) Timer.

Procedure:

1) Pipet 1.0 ml Acetate buffer and 0.5 ml ONPG solution into glass tubes and pre-incubate at 37C. Prepare one tube for each sample to be assayed.
2) After solution has had 5-10 minutes to warm up, initiate the assay of the first sample as directed below. Initiate subsequent samples every 20 seconds.
3) Add 100 ul of solution to be assayed. Vortex up and down 5 times and return immediately to 37C incubator.
4) 15 minutes after initiating each assay, stop the reaction by adding 2.0 ml Na Carbonate solution. Vortex and hold at room temperature.
5) As soon as all assays have been stopped, begin reading the absorbance at 420nm in the spectrophotometer. Read one assay every 20 seconds, in the same order in which the assays were initiated. Record the Absorbance.

Glucose Oxidase Assay

Materials: 1) 00 mM MES-Na pH 5.7 (Sigma M3671 and NaOH) (100 ml); 2)15% Beta-D-Glucose (Sigma G5250) 20 ml (prepare 2-20 hrs prior to assay); 3) 0.5% AA

solution (Sigma A4382) (10 ml); 4)40 mM EHSPT (Sigma E8631) (10 ml); 5)1.8 mg/ml Peroxidase (Sigma P6782) (1 ml); 6) Cuvettes, glass tubes with stoppers, etc.

Equipment: 1) Inctronic II incubator at 37C (both sides); 2) Spectrophotometer set at 555nm and zeroed with water; and 3) Timer

Procedure:

1) Mix Assay Solution. The following is sufficient for 24 assays:
60 ml MES buffer; 12 ml glucose solution; 0.6 ml AA solution; 0.6 ml EHSPT solution; and 0.6 ml Peroxidase solution.
2) Transfer 3 ml Assay Solution to glass tubes and pre-incubate at 37C. Prepare one tube for each sample to be assayed.
3) After Assay Solution has had 5-10 minutes to warm up, initiate the assay of the first sample as directed below. Initiate subsequent samples every 20 seconds.
4) Add 50 ul of solution to be assayed to the tube with Assay Solution. Vortex up and down 5 times and return immediately to 37C incubator.
5) 7 minutes after initiating each assay, the absorbance at 555nm should be determined in the spectrophotometer, and the result recorded.

Results are presented graphically in Figures 16a and 16b.

Claims

1. A system for thermal processing of a heat-sensitive fluid material comprising:

a) a source of microwave energy having a frequency of greater than 1000 MHz and a power supply of greater than 10 kW;

b) a means for providing a flow stream of a heat-sensitive fluid material, said flow stream having a flow rate of greater than 80 L/hr;

c) a waveguide in microwave communication with said source of microwave energy, said wave guide adapted to receive a flow path for said flow stream within said wave guide; and

d) means for monitoring and controlling said processing by said system.

2. The system of claim 1, wherein said power supply is contained within a power supply module, said power supply module further comprising:

a) means for moving said power supply module to a location remote from said wave guide;

b) means for electronically communicating with said means for monitoring and controlling said processing by said system.

3. The system of claim 1, wherein said system further comprises means for pre-heating said heat-sensitive fluid material in said flow stream.

4. The system of claim 3, wherein said system further comprises a utility module, said utility module comprising:

a) a source of heat for said pre-heating means; and

b) means for electronically communicating with said means for monitoring and controlling said processing by said system.

5. The system of claim 1, wherein said system further comprises means for cooling said heat-sensitive fluid material in said flow stream.

6. The system of claim 5, wherein said system further comprises a utility module, said utility module comprising:

a) a source of coolant for said cooling means; and

b) means for electronically communicating with said means for monitoring and controlling said processing in said system.

7. The system of any one of claims 4 and 6, wherein said utility module is remote from said microwave waveguide.

8. The system of claim 1, wherein said system further comprises means for measuring directly the temperature of said fluid stream.

9. The system of claim 1, wherein said means for monitoring and controlling said processing in said system comprise a user interface remote from said waveguide for remote monitoring of said system.

10. The system of claim 1, further comprising means for monitoring leakage of microwave energy from said waveguide.

11. The system of claim 1, further comprising means for controlling leakage of microwave energy from said waveguide.

12. The system of claim 11, wherein said means for controlling leakage comprise multiple clamps attached to a single bar characterized in that clamping and unclamping of said multiple clamps is leveraged using said single bar.

13. The system of claim 11, wherein said waveguide comprises an applicator region, and said means for controlling leakage comprises an air impermeable pressure window between said waveguide and said applicator region of said waveguide.

14. The system of claim 13, wherein said waveguide applicator region comprises a conductive gasket and a quarter wave choke.

15. The system of claim 1, further comprising means for injecting a fluid sample of at least 1500 liters per day into said flow stream.

16. The system of claim 1, wherein said flow stream has a flow rate of at least 300 liters/hour.

17. The system of claim 1, wherein said flow path for said flow stream within said waveguide is secured to a removable plate.

18. The system of claim 1, wherein said source of microwave energy having a frequency of greater than 1000 MHz has a power of greater than 20 kW.

19. The system of claim 1, wherein said source of microwave energy having a frequency of greater than 1000 MHz has a power of greater than 30 kW.

20. The system of claim 1, wherein said source of microwave energy having a frequency of greater than 1000 MHz has a power of greater than 10 kW and less than 100 kW.

21. A method of thermally reducing a micro-organism or pathogenic agent in a fluid sample of a heat-sensitive material, said method comprising the steps of:

a) providing a heat-sensitive fluid in a fluid flow stream having a flow rate of greater than 80 liters per hour;

b) exposing said fluid flow stream to microwave energy of greater then 1000 MHz for a pre-selected time sufficient to raise the temperature of said fluid in said flow stream to a pre-selected temperature so as to reduce or inactivate the micro-organism or pathogenic agent without substantial alteration of desirable properties of the material in said fluid; and

c) rapidly cooling said fluid flow stream.

22. The method of claim 21, wherein the frequency of said microwave energy is within the S band spectrum.

23. The method of claim 21, wherein the frequency of said microwave energy is about 2450 +/- 50 MHz.

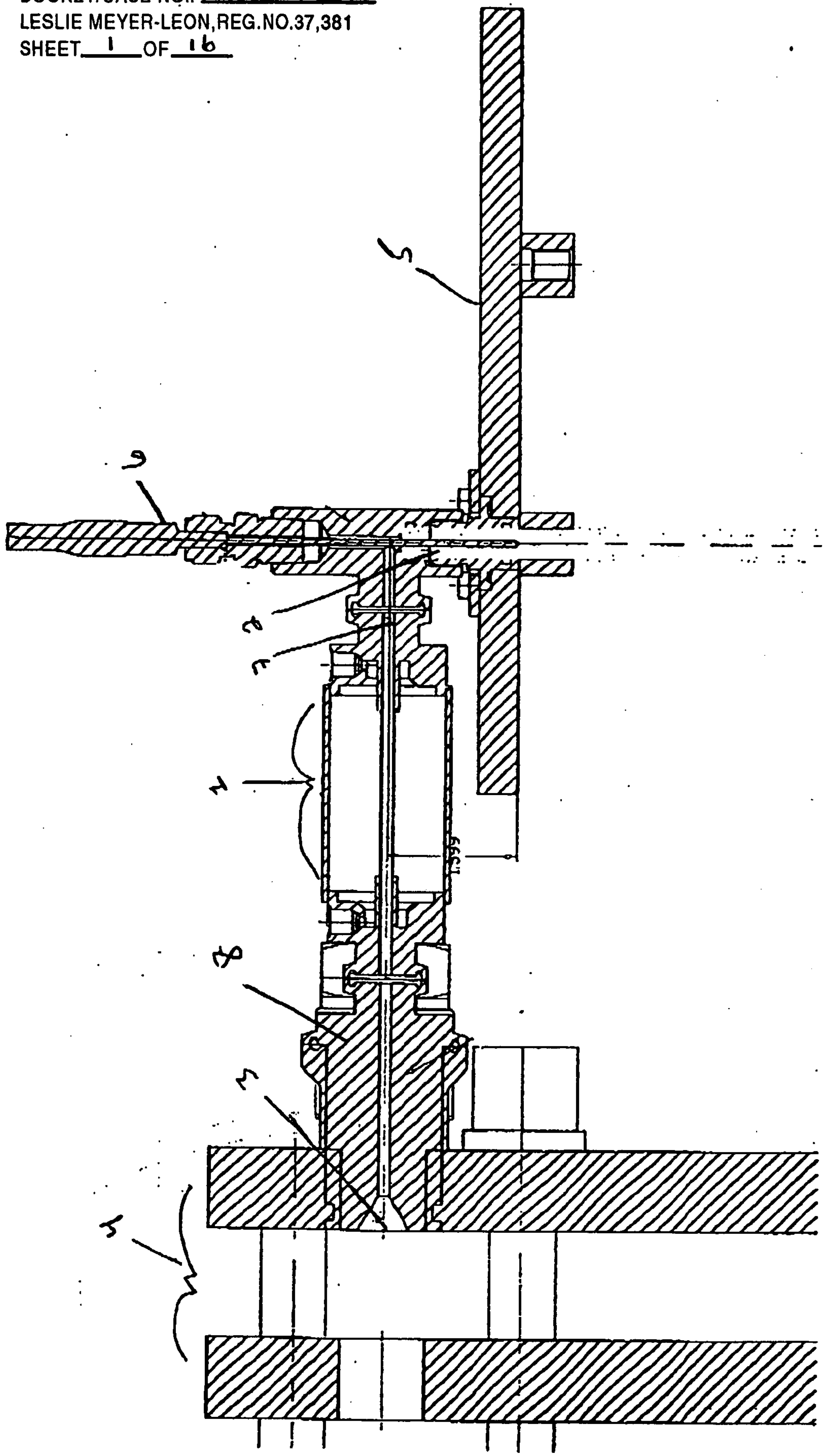
24. The method of claim 21, wherein said pre-selected time for exposing said fluid flow stream to microwave energy is less than 0.5 second and said flow rate is greater than 80 liters per hour.

ABSTRACT

The invention features a system for the continuous, high-temperature, short-time heat treatment of biological materials that is suitable for large scale production at rapid flow rates.

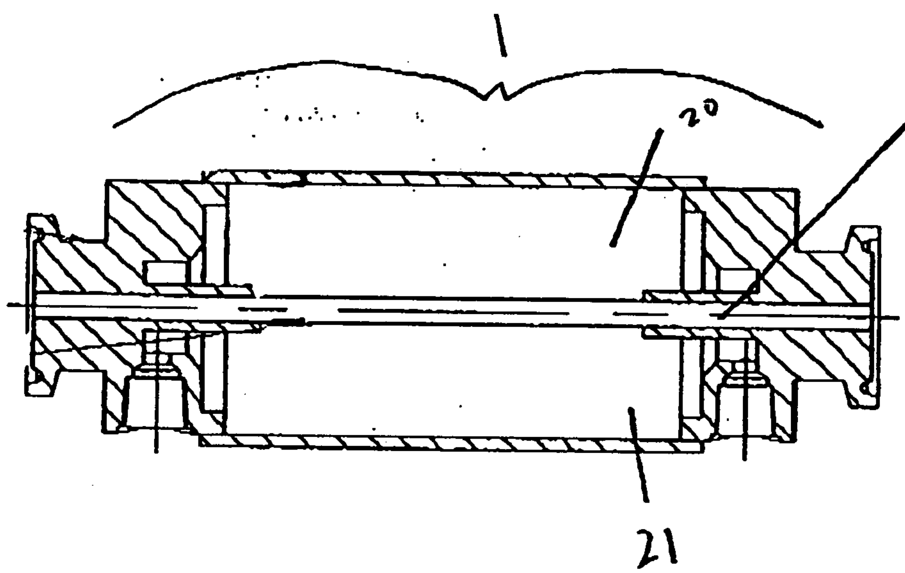
TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON, REG.NO.37,381
SHEET 1 OF 16

1

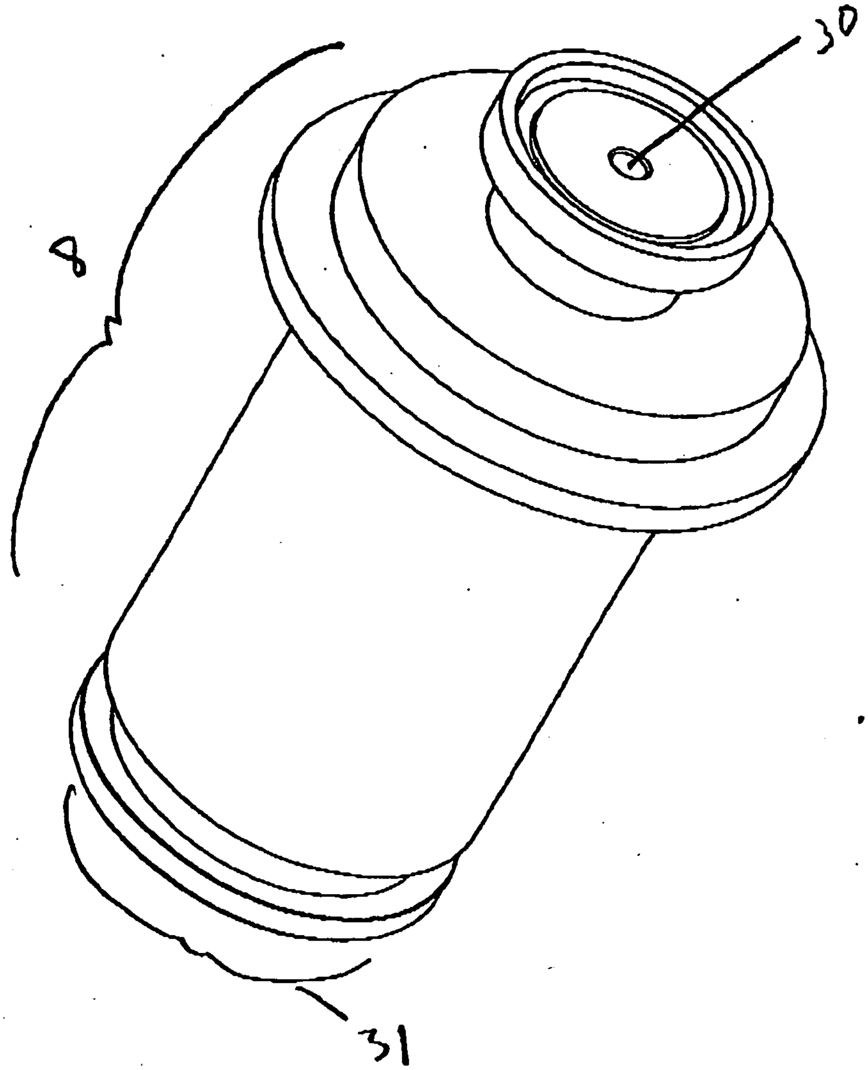


TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Cham et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON,REG.NO.37,381
SHEET 2 OF 16

2



TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON, REG.NO.37,381
SHEET 3 OF 16



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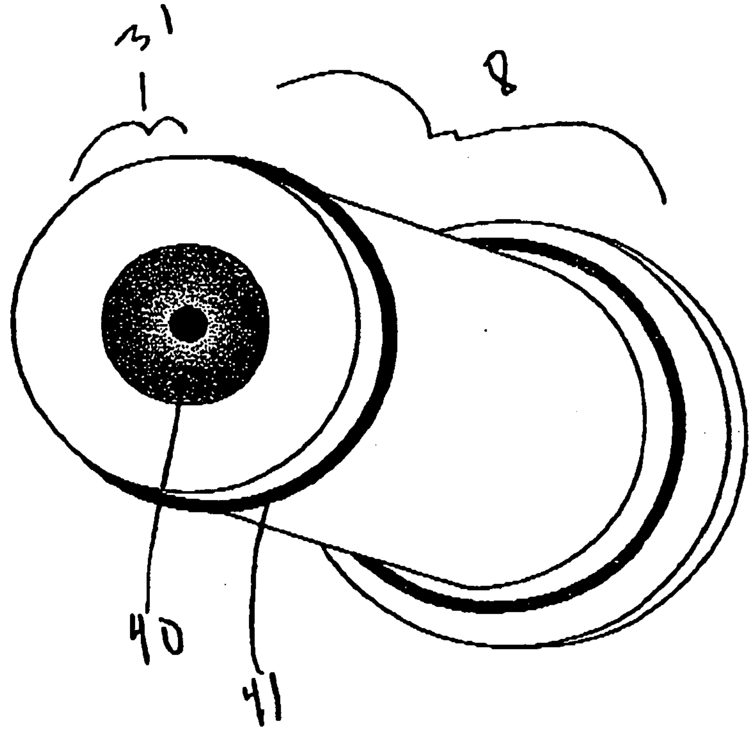
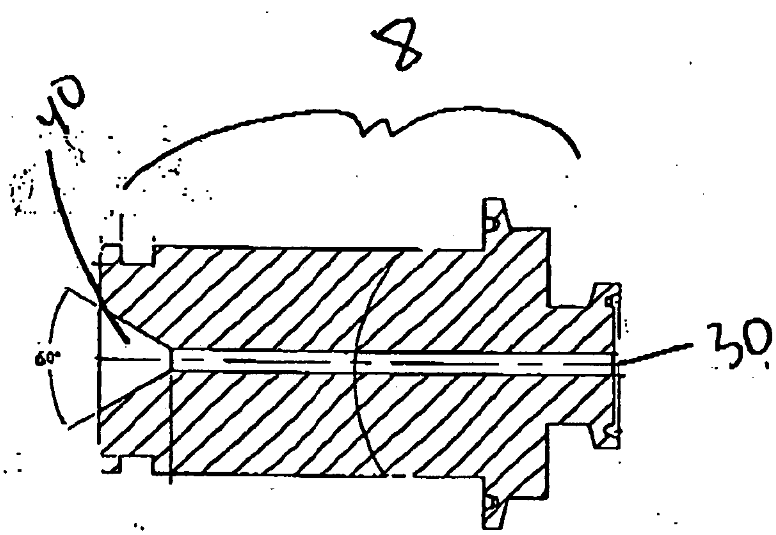


TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Chen et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON, REG.NO.37,381



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INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON, REG.NO.37,381
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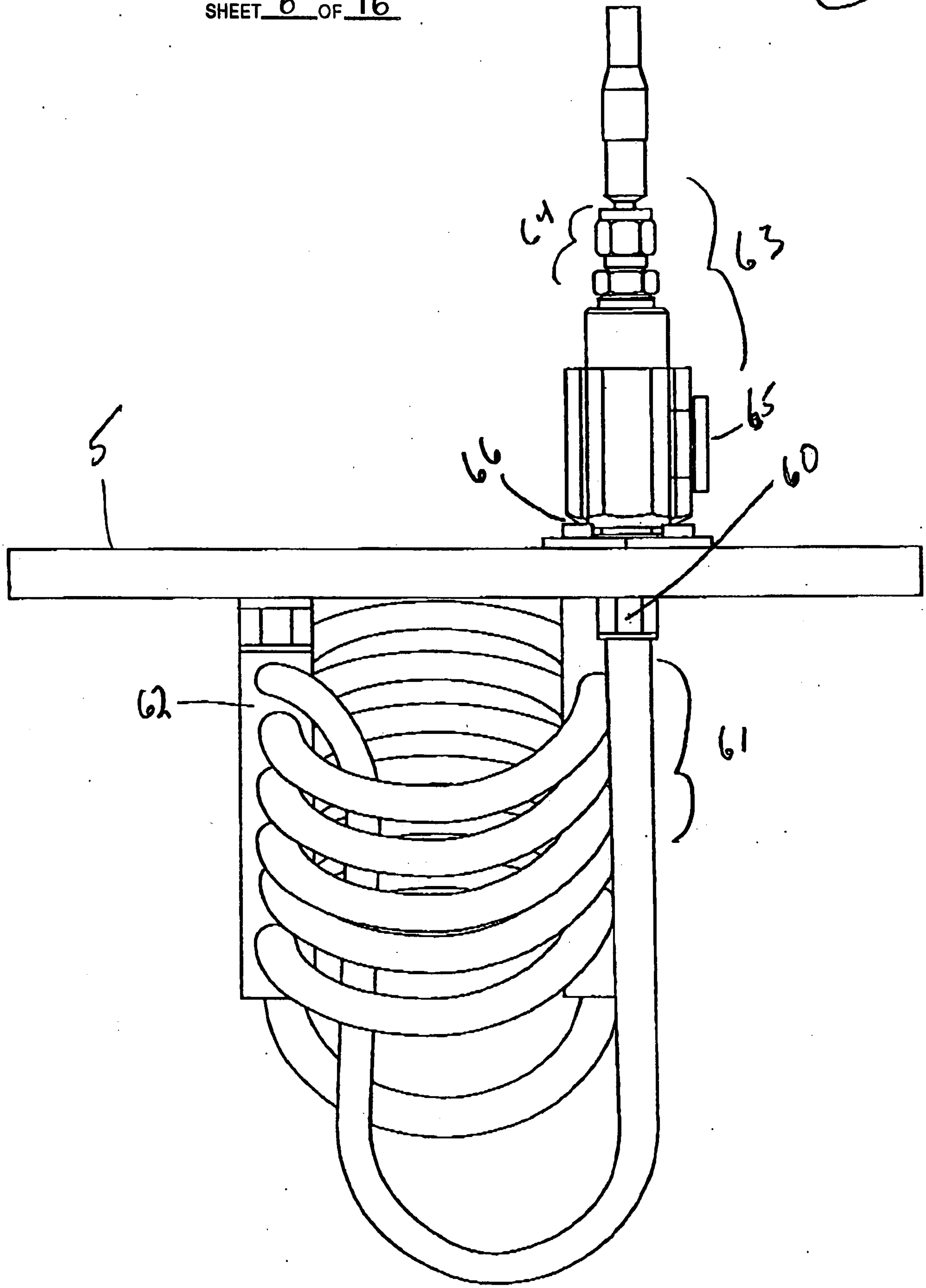

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INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON, REG.NO.37,381
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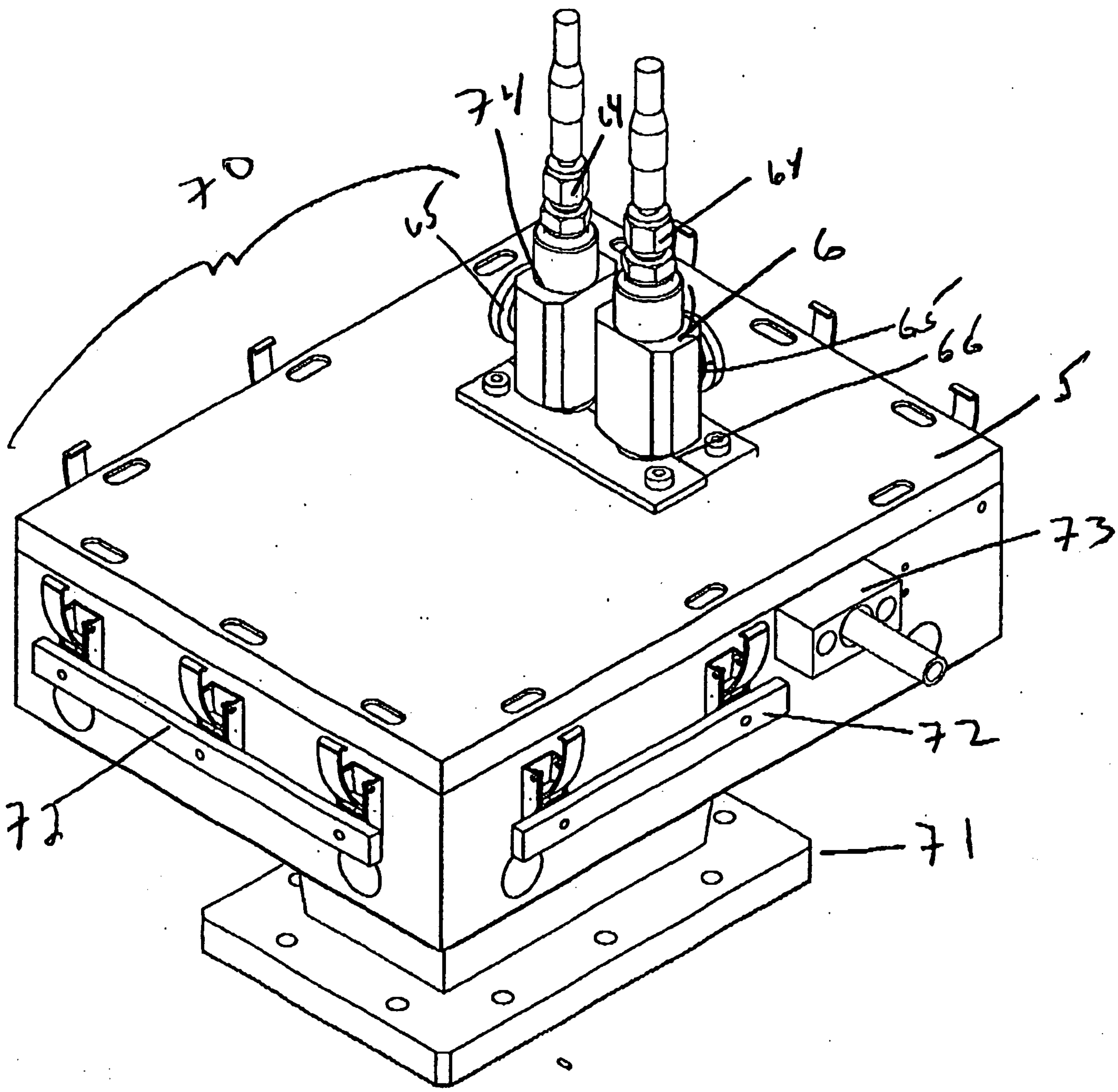

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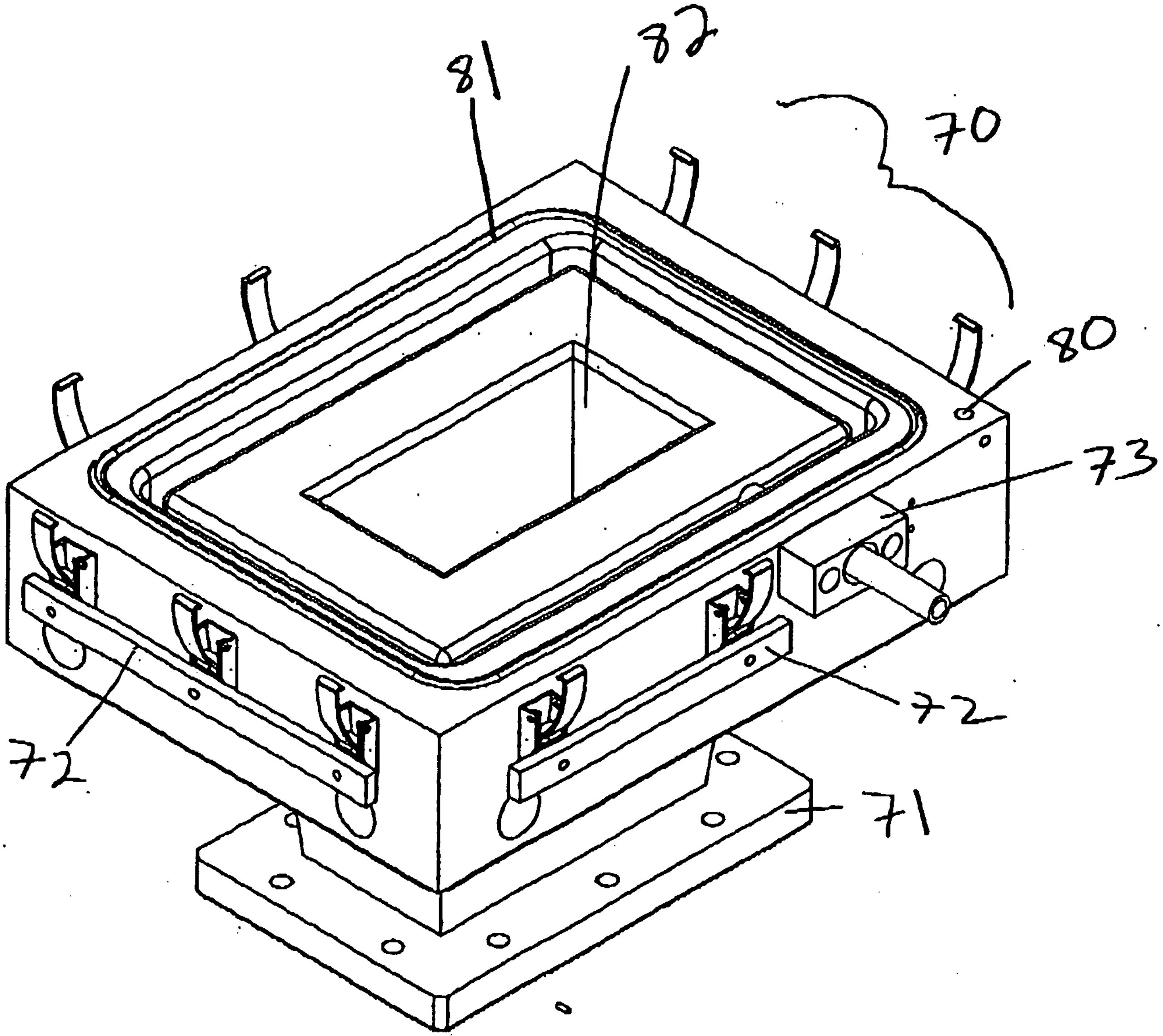

TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0650-027US1
LESLIE MEYER-LEON,REG.NO.37,381
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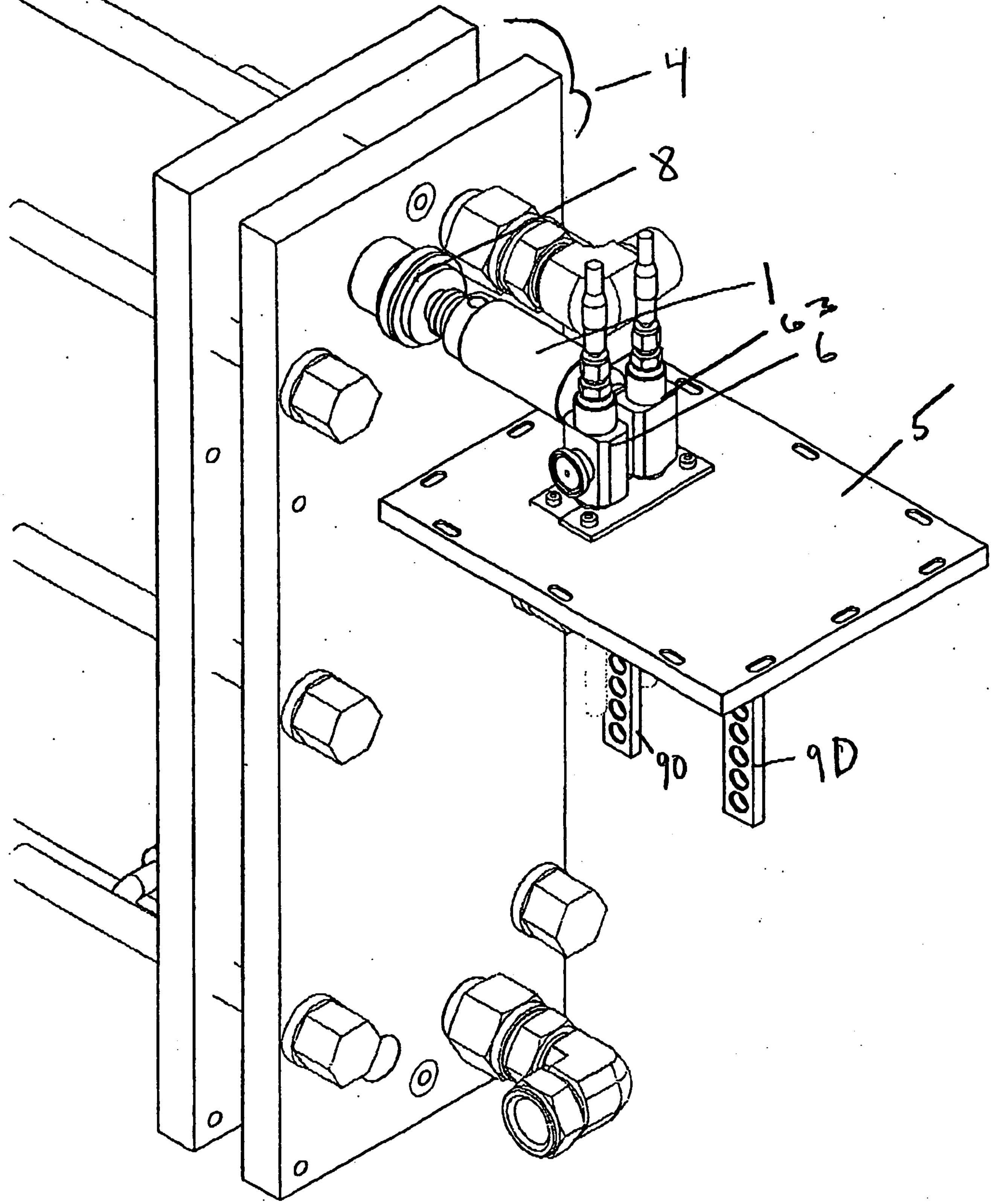

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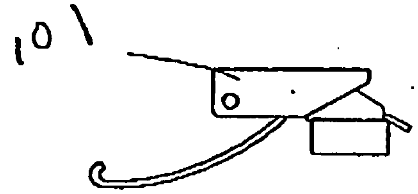

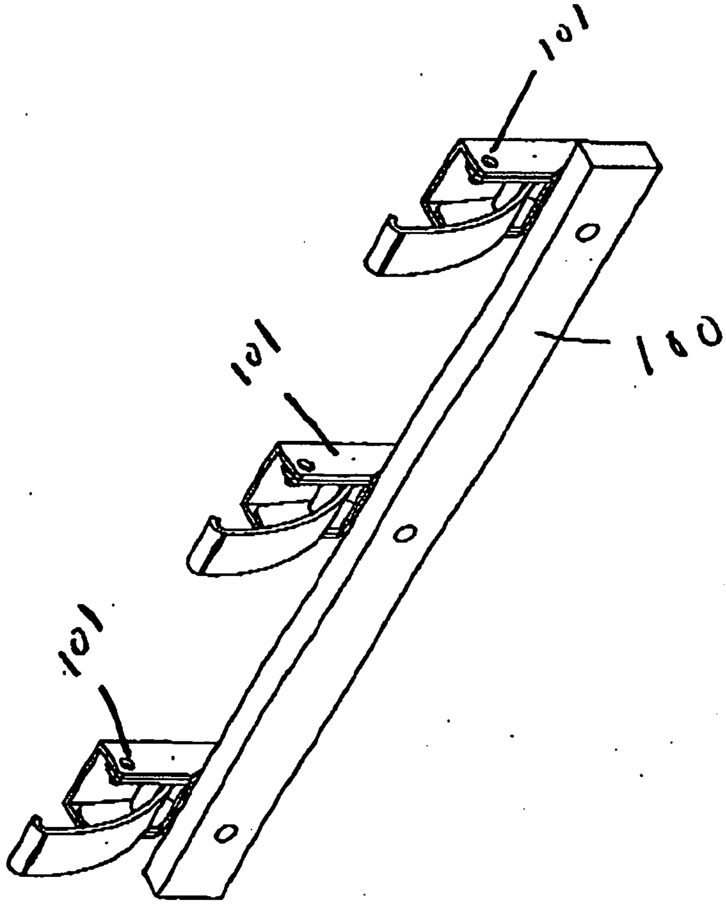

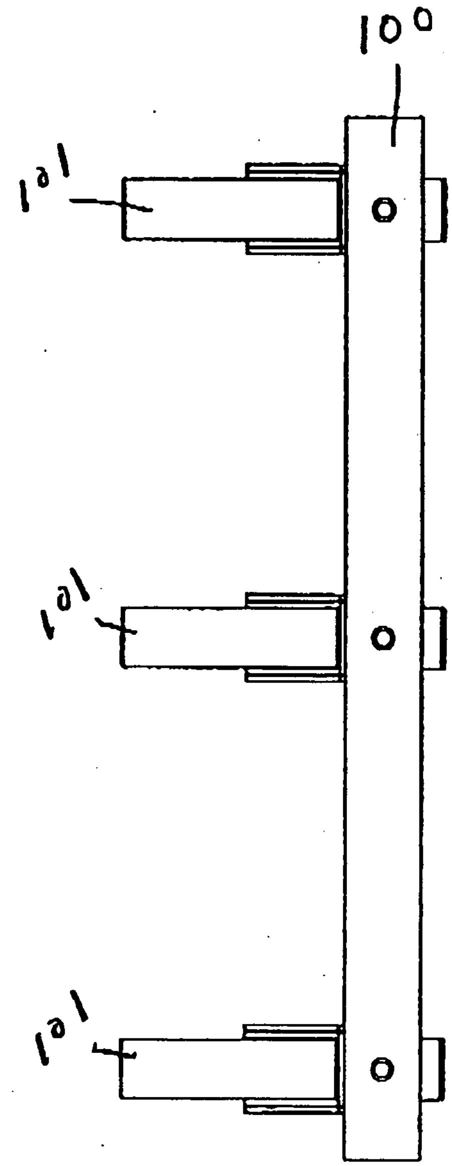

TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0650-027US1
LESLIE MEYER-LEON, REG.NO.37,381
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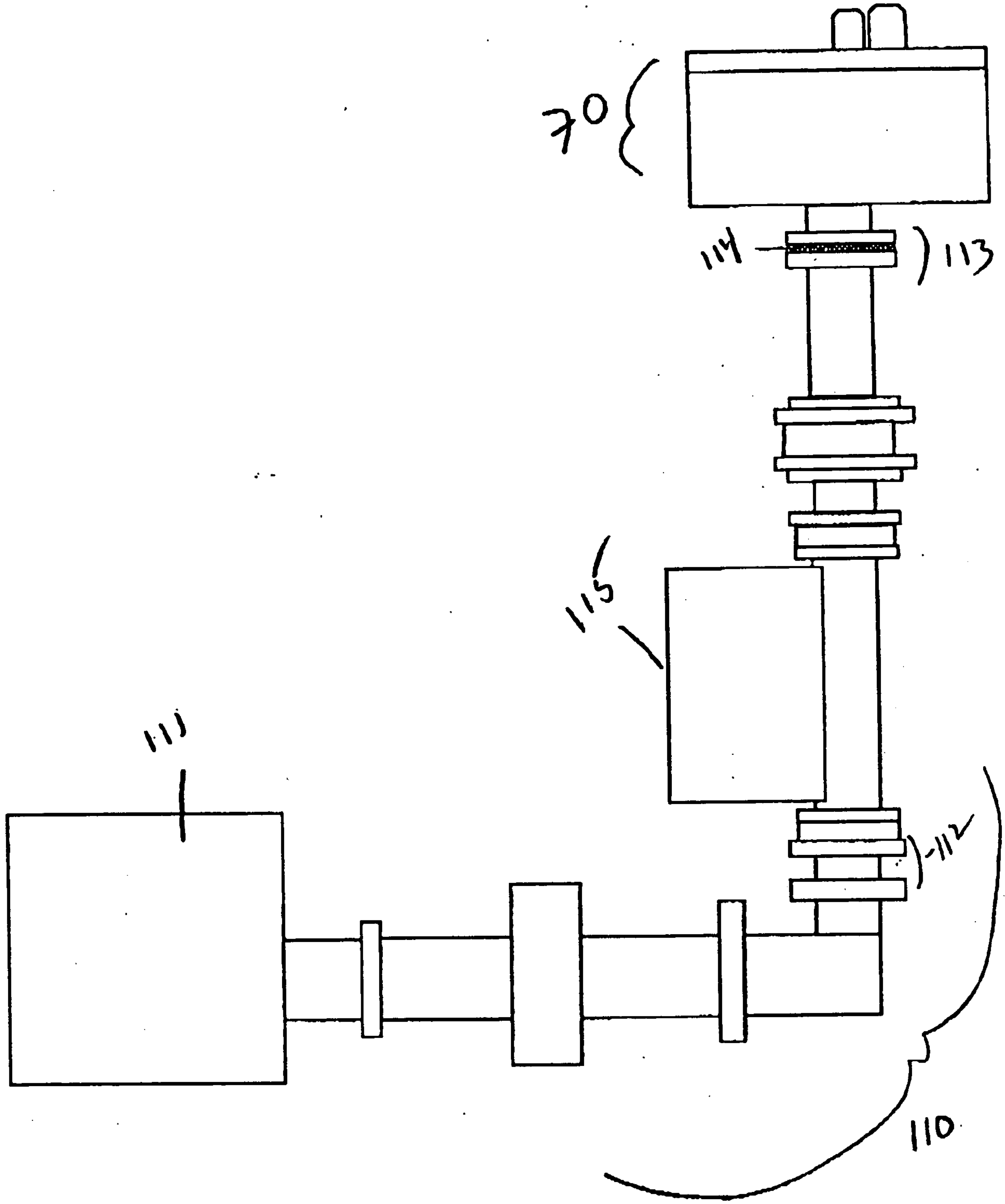

TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Chamet al.
DOCKET/CASE NO.: 0656-0274US1
LESLIE MEYER-LEON, REG.NO.37,381
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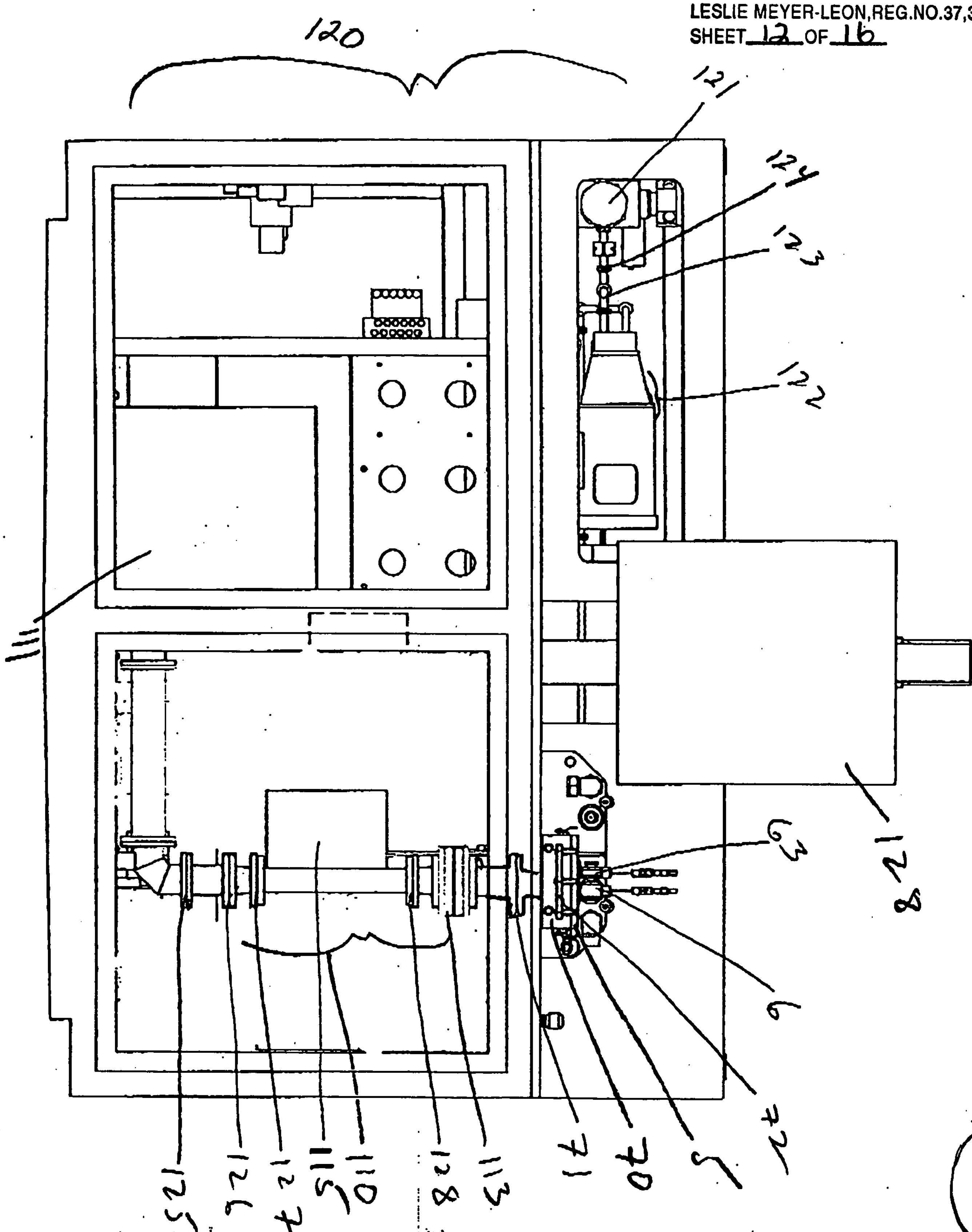

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TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Cham et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON, REG.NO.37,381
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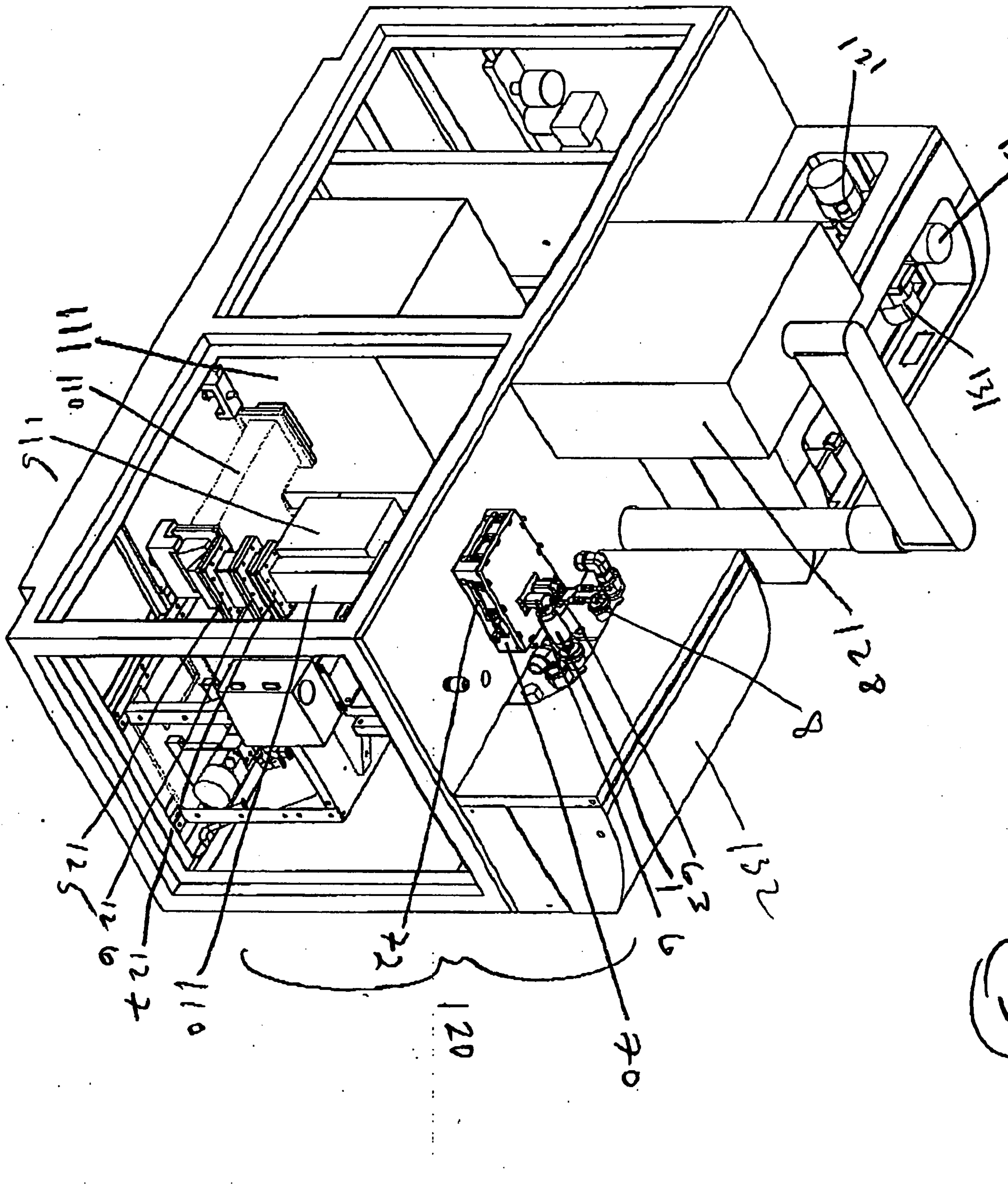

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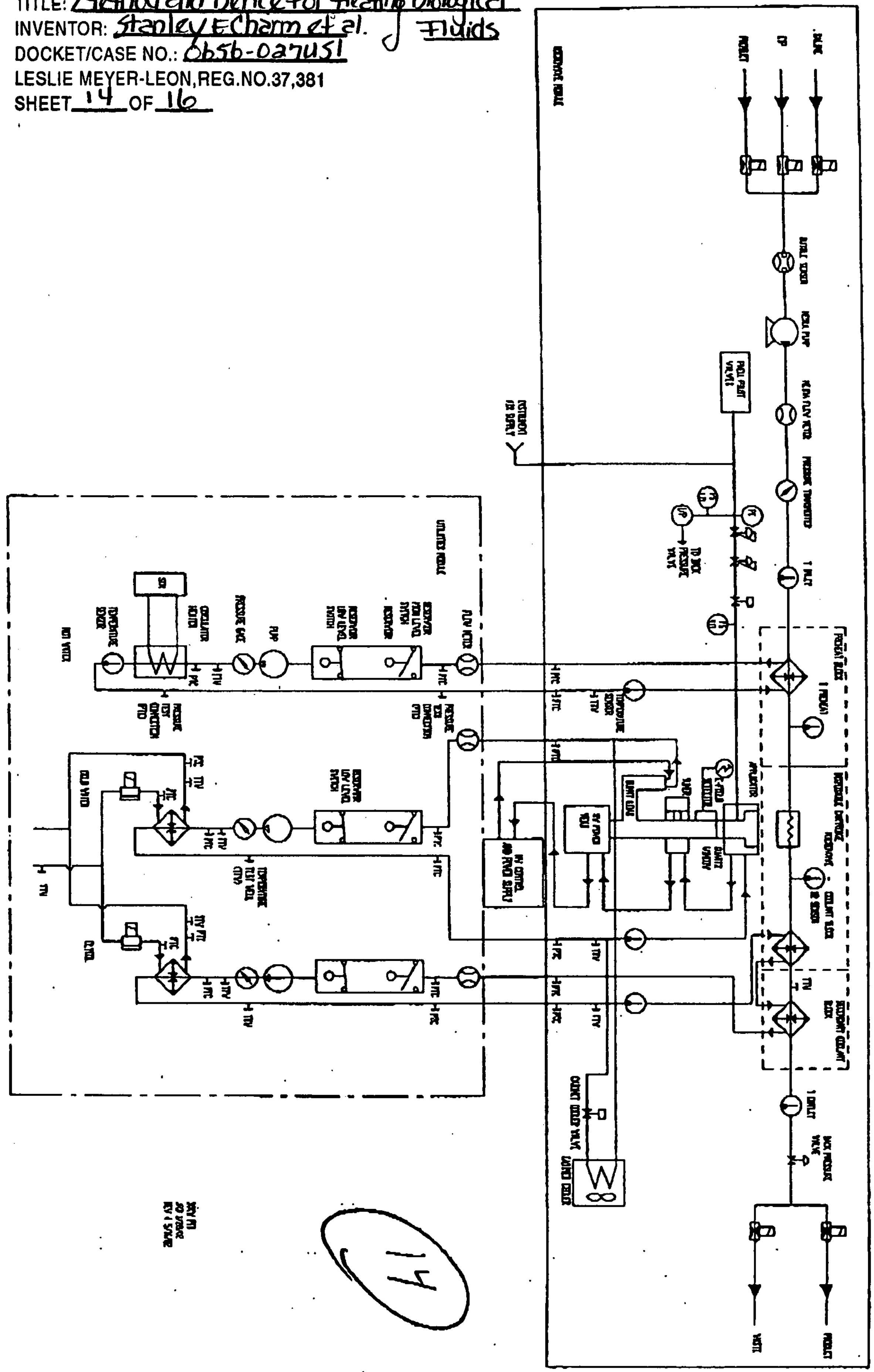
TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E Charm et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON,REG.NO.37,381
SHEET 14 OF 16



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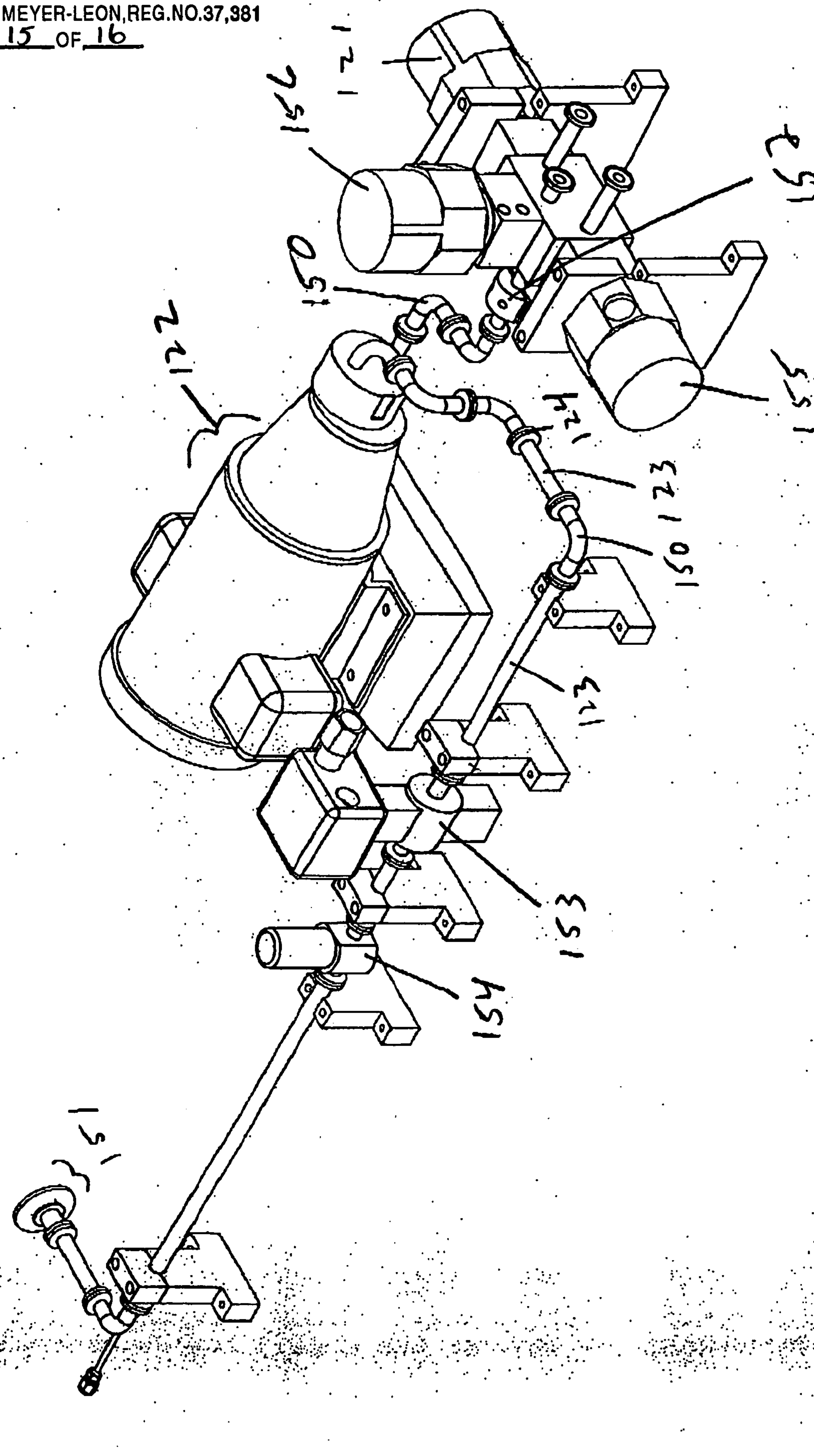
15

TITLE: Method and Device for Heating Biological Fluids
INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0650-027US1
LESLIE MEYER-LEON, REG.NO.37,381
SHEET 15 OF 16



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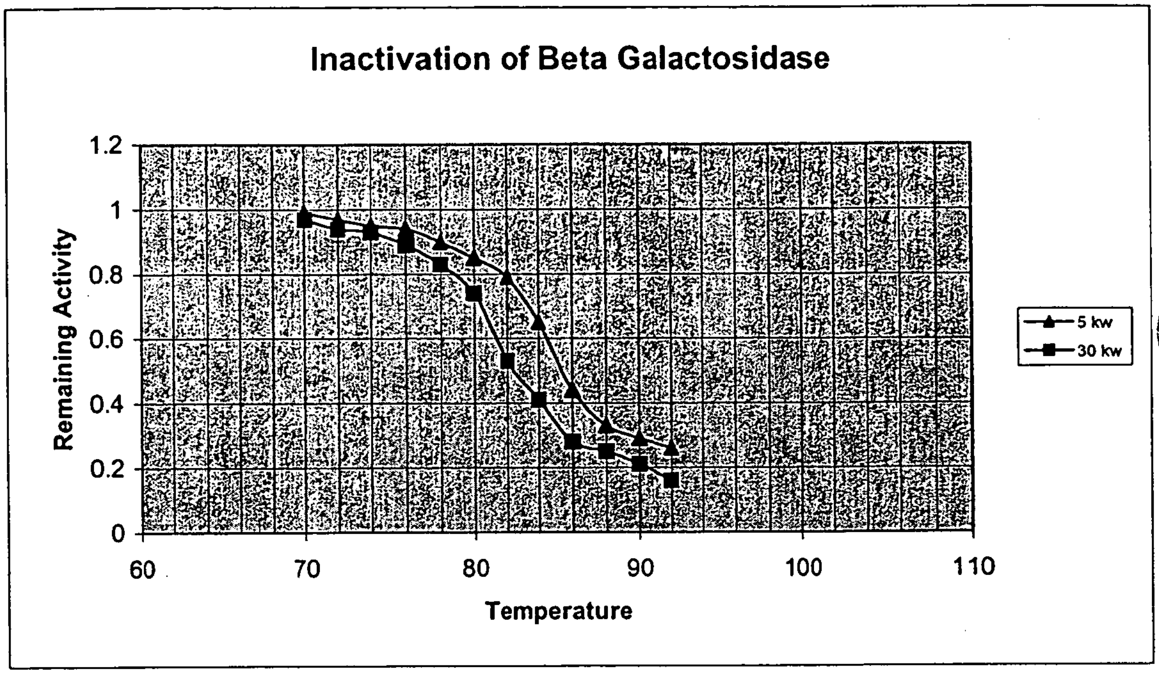
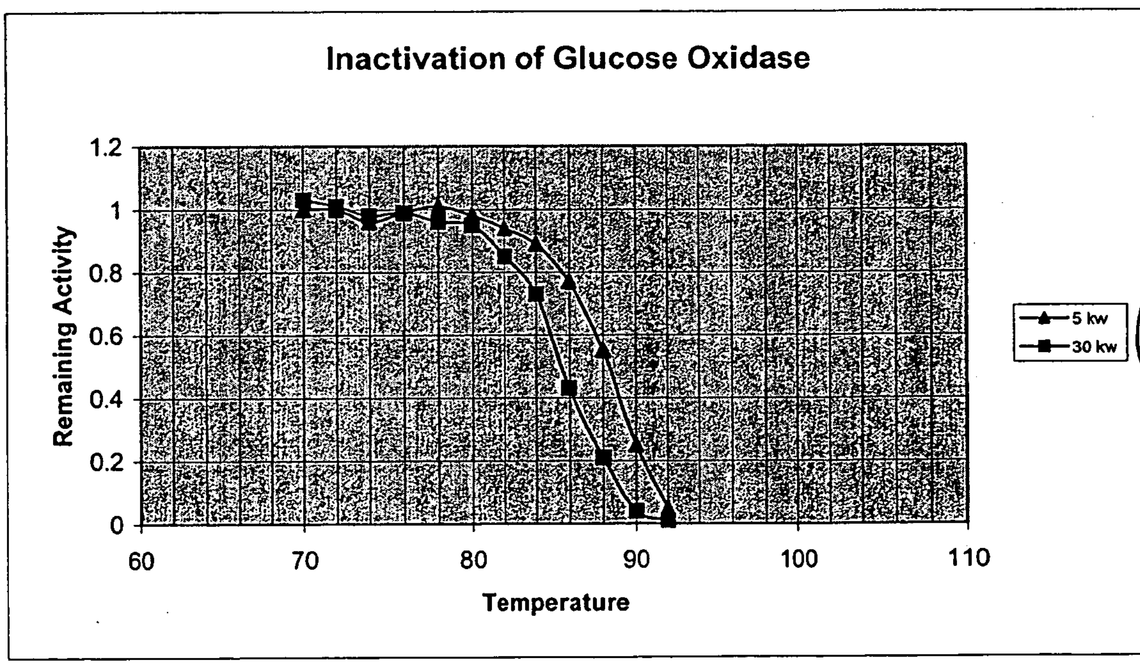
INVENTOR: Stanley E. Charm et al.
DOCKET/CASE NO.: 0656-027US1
LESLIE MEYER-LEON,REG.NO.37,381
SHEET 16 OF 16



16a



16b